Some reactions of 3-chloroisoindolium salts with nucleophiles: access to isoindole derivatives and ellipticine analogues as potential antiviral agents

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3-Chloro-2-substituted-1-oxoisoindolium hexachloroantimonate **(1)** reacted with water, ethanol and dimethylcyanamide to give the corresponding phthalimide derivatives **2**, **3** and **4** respectively. Reaction of **1a** with nitriles afforded the intermediate 2-azoniaallene salts **5** which underwent cyclisation reaction upon heating to furnish the ellipticine analogues **6**. The biological activities of **6a–e** against HIV-1 and HBV viruses were determined.

Keywords: isoindolium salts, isoindole derivatives, 2-azoniaallene salts, cyclic *N*-acyliminium salts, ellipticine analogues, HIV-1 and HBV viruses

During the past decade *N*-acyl iminium ions have found wide application in the construction of natural and non-natural products of possible biological interest. Amongst these are the syntheses of the indole alkaloid (–)-ajmalicine[1], the gelsemium alkaloids, (±) gelsemine,[2] (+)-gelesdine,[3] the stemona alkaloid (+) croomine,[4] the pyrrolopyrimidinone alkaloid (±)-aglaiastatin,[5] the guanidinium alkaloid (–)-ptilomycalin,[6] the marine-derived antitumour agent ecteina scidin,[7] the antibiotic (+)-streptazolin,[8] and the pyrrolidine-5,5-*trans*-lactam derivatives, which showed activity against Hepatitis C virus NS3/4A protease.[9] In the β-lactam field, carbapenems[10], carbacephems[11], loracarbacef[12], trinem antibiotics and γ-lactam analogues of claviminic acid[13] have been prepared by *N*-acyliminium chemistry.

Ellipticine, (5, 11-dimethyl-6H-pyrido[4,3 –*b*]carbazole), (Fig. 1) is a naturally occurring alkaloid isolated from the leaves of *Ochrasia elliptica* Labill[14]. The discovery of its antitumour activity in 1967 has led to an explosion of synthetic, biological and pharmacological studies.[15] Several ellipticine analogues have been used as non-nucleoside reverse transcriptase inhibitors,[16,17] DNA intercalators[18-25] and antioxidants.[26]

In continuation of our interest in the chemistry of *N*-acyliminium and 2-azoniaallene salts,[27–33] we now report some reactions of the cyclic *N*-acyliminium salt with diverse nucleophiles as an access to ellipticine analogues and other useful products.

Results and discussion

The starting material 3–chloro–2–substituted-1–oxoisoindolium hexachloroantimonate **(1)** could be prepared as described in the literature[31] by adding a solution of $SbCl_5$ in CH_2Cl_2 to a cold (–30°C) mixture of an isocyanate and benzotrichloride in CH_2Cl_2 which afforded a yellowish orange precipitate. This salt is extremely sensitive toward nucleophiles. With traces of water or a better aqueous base, the phthalimides **2** are formed. On addition of a large excess of ethyl alcohol to a cold (–10°C) suspension of **1** in CH_2Cl_2, the orange solid dissolves immediately. Subsequent hydrolysis with aqueous NaOH and separation of the organic layer repeatedly with CH_2Cl_2 furnishes 3,3-diethoxy-2-substituted-1-oxoisoindoles **(3)**.

The structure assignments of **3** are based on spectroscopic (IR, ^1H and ^{13}C NMR) and elemental analysis data. IR spectra showed absorption bands in the range of 1713–1731cm^{-1} (C=O). In the ^1H NMR spectra of **3**, diastereotopic CH_2 protons are observed. The high field (2.81–2.95 ppm) resonance of CH_2 protons of compound **3d** is probably attributable to the anisotropic effect of the phenyl group in position 2. Signals

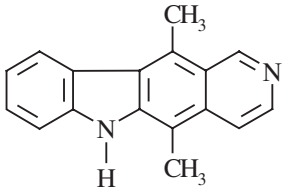

Fig. 1 Ellipticine.

in the range of 102.1–111.5 ppm in the ^{13}C NMR spectra ($CDCl_3$) are assigned to the saturated ketal carbon atoms.

3-Chloro-1-oxoisoindolium salt **1** is regarded as an α-chlorocarbenium ion. It can react with nitriles according to the *Ritter reaction* to give initially an α-chloronitrilium salt, which rearranges via a 1,3-chlorotropic shift to the thermodynamically more stable 2-azoniaallene salt. Thus, it reacted with two equivalents of the electron-rich nitrile dimethylcyanamide to produce 2-azoniaallene salts **4**. The spectroscopic data of **4** were consistent with the assigned structures. The IR spectra showed absorption bands around 1770 and 1680 cm^{-1} (KBr) characteristic of (C=O) and (C=N$^+$) respectively. The ^1H NMR spectrum of **4a** (CD_3CN) showed four signals for CH_3 groups indicating hindered rotation of the two $N(CH_3)_2$ groups.

With less reactive nitriles, **1a** reacted in a ratio 1:1 in boiling dichloroethane affording *in situ* the intermediate 2-azoniaallene salt **5**. Upon prolonged heating, it cyclised to the tetracyclic compound oxoisoindolo[2,1-a] quinazolinium hexachloroantimonate (**6**) which is considered as an ellipticine analogue. Reaction of α-chlorocarbenium ions with nitriles have been recently described by us.[27-29] A mechanism explaining the formation of **6** is proposed in Scheme 2. The constitution of **6** is derived from spectroscopic data (see experimental).

In conclusion, while several steps are required for the synthesis of ellipticine[34, 35] or its analogues[20, 36-39] we describe a facile one-pot synthesis of a new series of ellipticine analogues and other useful compounds.

Antiviral activity

Compounds **6a–e** were examined for possible antiviral activity against HIV-1 strain HTLV-IIIB and HBV cell culture (Hep G2 2.2. 15).[40]

(a) Against HIV: The strain of HIV-1 was propagated in H9 cells[41] at 37°C, 5% CO_2 using RPMI 1640 with 10% heat-inactivated fetal calf serum (FCS) and antibiotics (growth medium). The culture supernatant was filtered (0.45 nm), aliquoted, and stored at –80 °C until use. The MT-4 cells, which were used as target cells, were incubated with virus (0.005 MOI) for 2h, washed, and added in a proportion of 1:10

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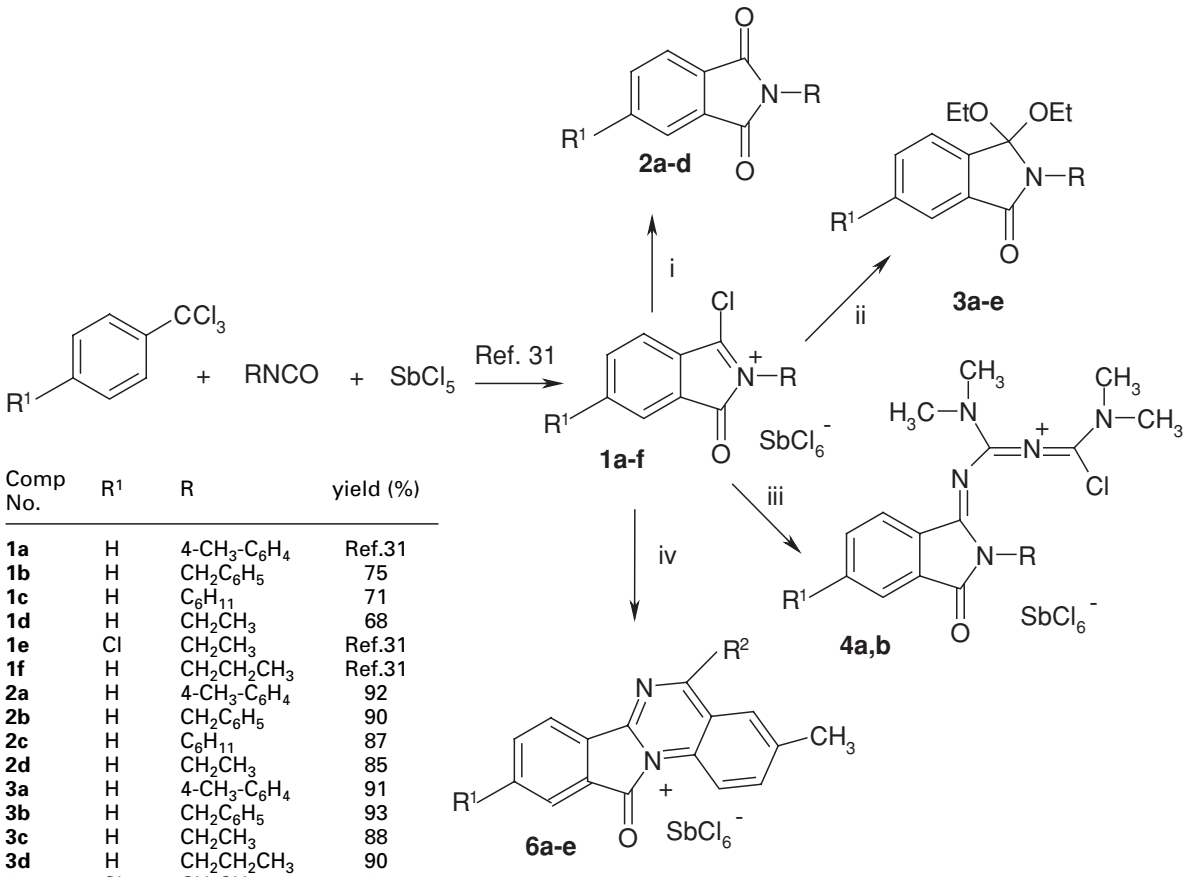
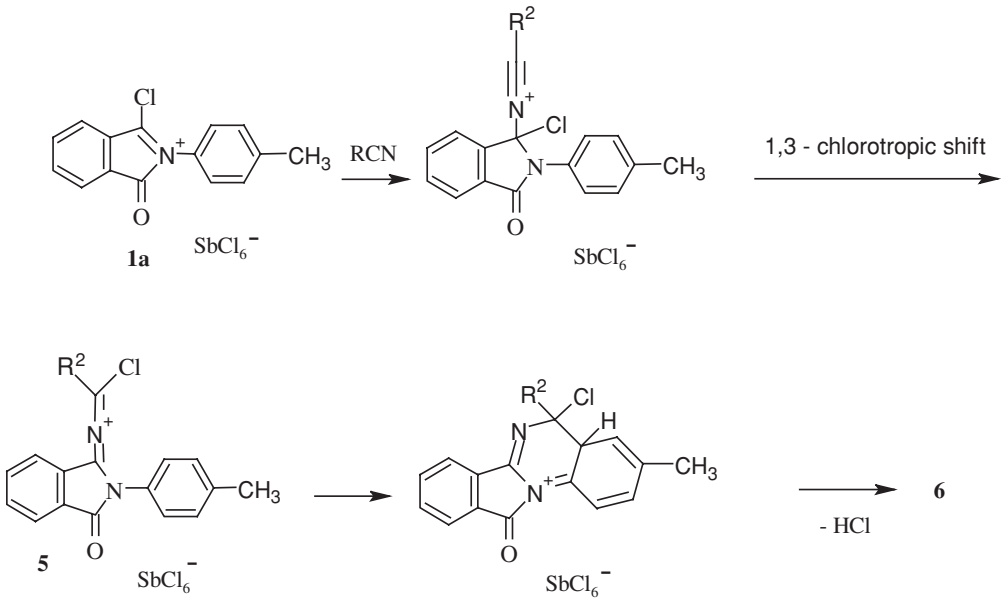


Comp No.	R^1	R	yield (%)
1a	H	4-CH_3-C_6H_4	Ref.31
1b	H	$CH_2C_6H_5$	75
1c	H	C_6H_{11}	71
1d	H	CH_2CH_3	68
1e	Cl	CH_2CH_3	Ref.31
1f	H	$CH_2CH_2CH_3$	Ref.31
2a	H	4-CH_3-C_6H_4	92
2b	H	$CH_2C_6H_5$	90
2c	H	C_6H_{11}	87
2d	H	CH_2CH_3	85
3a	H	4-CH_3-C_6H_4	91
3b	H	$CH_2C_6H_5$	93
3c	H	CH_2CH_3	88
3d	H	$CH_2CH_2CH_3$	90
3e	Cl	CH_2CH_3	87
4a	H	$CH_2C_6H_5$	56
4b	H	CH_2CH_3	65
		R^2	
6a	H	SCH_3	52
6b	H	C_6H_5	64
6c	H	2-CH_3-C_6H_4	66
6d	H	4-CH_3-C_6H_4	71
6e	H	1-naphthyl	88

Scheme 1 Reagents and conditions: i-aq.$NaHCO_3$; ii-excess EtOH, –10°C; iii–$(CH_3)_2NCN$, CH_2Cl_2, –10 to 23°C; iv–R^2CN, $ClCH_2CH_2Cl$, 83°C.



Scheme 2

to uninfected cells which had been preincubated in growth medium containing the test compound for six days in parallel with virus-infected control cultures without compound added. Expression of HIV in the culture medium was quantified by HIV antigen detection assay ELISA.[42]

(b) Against HBV: Maintenance media were added to the cell culture (Hep G2 2.2. 15) together with the tested compounds. The supernatant liquid was collected after one week. The DNA replication was estimated by the PCR (polymerase chain reaction) technique. The percentage inhibition could be calculated by the relation between the blank experiment (containing maintenance media without the tested compounds) and the results obtained after the mentioned period. The percentage cytotoxicity could be estimated by the relation between the number of the living and dead cells after three weeks counted by the haemocytometer. Compounds **6a–e** did not show any significant activity against HIV or HBV at non-toxic concentrations.

Experimental

All solvents were dried by standard methods. All experiments were carried out with exclusion of moisture. Melting points were determined with a Kofler block apparatus and are uncorrected. IR spectra were recorded with Perkin-Elmer Model 1720 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were determined with Varian Gemini 2000 and Bruker AC-250 FT spectrometers. The chemical shifts in ppm are expressed on the δ scale using tetramethylsilane as internal standard. Coupling constants are giving in Hz. Microanalyses were performed in the unit of microanalyses at the Universities of Cairo (Egypt) and Odense (Denmark). The biological activity was determined in Retrovirus Laboratory, State Serum Institute, Copenhagen (Denmark) and National Liver Institute, Menoufia University, Egypt.

N-substituted 3-chloro-1-oxoisoindolium hexachloroantimonate **(1a–e);** *general procedure*
From benzotrichloride derivatives, $SbCl_5$, and appropriate isocyanate in CH_2Cl_2 or 1,2-dichloroethane at –30 °C as described in ref. 31.[31]

3-Chloro-2-(4-methylphenyl)-1-oxoisoindolium hexachloroantimonate **(1a)**: From benzotrichloride, $SbCl_5$ and *p*-tolylisocyanate as described in lit.[31]

3-Chloro-2-benzyl-1-oxoisoindolium hexachloroantimonate **(1b)**: A solution of $SbCl_5$ (2.99 g, 10 mmol) in CH_2Cl_2 (10 ml) was added dropwise to a cold (–30 °C) solution of benzotrichloride (1.96 g, 10 mmol) and benzylisocyanate (1.33 g, 10 mmol) in CH_2Cl_2 (30 ml). After stirring at –30 °C for 10min and then at 23 °C for 3h a moisture sensitive yellow precipitate was filtered off and washed with CH_2Cl_2. Crystallisation from hot 1,2-dichloroethane afforded yellow fine crystals.

Yield: 4.44 g (75%); m.p. 220–221 °C. IR (Nujol) : ν = 1595, 1713, 1805 cm^{-1}. ^{1}H NMR (CD_3CN): δ = 5.40 (s, 2H, CH_2), 7.46–8.21 (m, 9H, aryl-H). ^{13}C NMR (CD_3CN): δ = 49.12 (CH2), 117.83, 129.16, 129.35, 129.72, 129.80, 130.00, 130.62, 133.57, 138.20, 140.73 (aryl), 162.93, 184.25 (C=O, C=N). Anal. calcd for $C_{15}H_{11}Cl_7NOSb$ (591.17): C, 30.47; H, 1.88; N, 2.37. Found: C, 30.78; H, 1.51; N, 2.11 .

3-Chloro-2-cyclohexyl-1-oxoisoindolium hexachloroantimonate **(1c)**: From benzotrichloride (1.96 g, 10 mmol), $SbCl_5$ (2.99 g, 10 mmol) and cyclohexylisocyanate (1.25 g,10 mmol) as described for **1b**.

Yield: 4.14 g (71%); yellow powder; m.p. 215–217 °C; IR (Nujol): ν = 1586, 1717, 1813 cm^{-1}. ^{1}H NMR (CD_3CN): δ = 1.46–2.26 (m, 10H), 4.57–4.69 (m, 1H, cyclohexyl-H), 8.09–8.20 (m, 4H, aryl-H). ^{13}C NMR (CD_3CN): δ = 25.31, 26.00, 30.17, 61.76 (cyclohexyl), 129.49, 129.90, 134.62, 135.71, 138.93, 141.10 (aryl), 163.93, 183.79 (C=O, C=N). Anal. Calcd for $C_{14}H_{15}Cl_7NOSb$ (583.20): C, 28.83; H, 2.59; N, 2.40. Found: C, 28.63; H, 2.81; N, 2.15.

3-Chloro-2-ethyl-1-oxoisoindolium hexachloroantimonate **(1d)**: From benzotrichloride (1.96 g, 10 mmol), $SbCl_5$ (2.99 g, 10 mmol) and ethylisocyanate (0.71 g, 10 mmol) as described for **1b**.

Yield: 3.60 g (68%); yellow powder; m.p. 205–207 °C; IR (Nujol): ν = 1598, 1679, 1825 cm^{-1}. ^{1}H NMR (CD_3CN): δ = 1.48 (t, 3H, *J* = 7.3, CH_3), 4.26 (q, 2H, *J* = 7.2, CH_2), 8.09–8.23 (m, 4H, aryl-H). ^{13}C NMR (CD_3CN): δ = 13.12 (CH_3), 42.53 (CH_2), 126.82, 129.51, 130.14, 134.45, 139.22, 141.42 (aryl), 163.73, 183.84 (C=O, C=N). Anal. Calcd for $C_{10}H_9Cl_7NOSb$ (529.10): C, 22.70; H, 1.71; N, 2.65. Found: C, 22.43; H, 1.82; N, 2.33.

3,6-Dichloro-2-ethyl-1-oxoisoindolium hexachloroantimonate **(1e)**: From 4-chlorobenzotrichloride, $SbCl_5$ and ethylisocyanate as described in ref. 31.

3-Chloro-2-propyl-1-oxoisoindolium hexachloroantimonate **(1f)**: From benzotrichloride, $SbCl_5$ and *n*-propylisocyanate as described in ref. 31.

N-substituted phthalimides **(2a–d)**; *general procedure*
A solution of $NaHCO_3$ in H_2O (1 N) was added to a suspension of **1** (5 mmol) in CH_2Cl_2 (20 ml) until no further CO_2 evolved. The organic layer was extracted with CH_2Cl_2 (2 × 10 ml) and dried over anhydrous Na_2SO_4. Filteration and evaporation of the solvent afforded a colourless powder, which could be crystallised from ethanol.

N-(4-methylphenyl) phthalimide **(2a)**: From **1a** (2.96 g, 5 mmol) as described before. Yield: 1.10 g (92%), m.p. 204–205 °C (lit.[43]: 201–202 °C). ^{1}H NMR ($CDCl_3$): δ = 2.41 (s, 3H, CH_3), 7.31 (s, 4H, aryl-H), 7.76–7.96 (m, 4H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 21.54 (CH_3), 124.00, 126.78, 129.29, 130.10, 132.16, 134.62, 138.50 (aryl), 167.75 (C=O).

N-benzylphthalimide **(2b)**: From **1b** (2.96 g, 5 mmol) as described for **2a**. Yield: 1.08 g (90%), m.p. 114–115 °C (lit.[44]: 113–114 °C). ^{1}H NMR ($CDCl_3$): δ = 4.74 (s, 2H, CH_2), 7.15–7.97 (m, 9H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 41.80 (CH_2), 123.52, 128.01, 128.80, 128.87, 132.31, 134.16,136.58 (aryl), 168.61 (C=O).

N-cyclohexylphthalimide **(2c)**: From **1c** (2.92 g, 5 mmol) as described for **2a**. yield: 1.00 g (87%), m.p. 166–168 °C (lit.[45]: 163–165 °C). ^{1}H NMR ($CDCl_3$): δ = 1.17–2.21 (m, 10H), 3.97–4.11 (m, 1H, cyclohexyl), 7.61–7.97 (m, 4H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 25.34, 26.24, 30.08, 51.09 (cyclohexyl), 123.18, 132.26, 133.92 (aryl), 168.61 (C=O).

N-ethylphthalimide **(2d)**: From **1d** (2.65 g, 5 mmol) as described for **2a**. yield: (0.75 g, 85%), m.p. 79–80 °C (lit.[46]: 77°C). ^{1}H NMR ($CDCl_3$): δ = 1.18 (t, 3H, *J* = 7.0 Hz, CH_3), 3.64 (q, 2H, *J* = 7.1Hz, CH_2), 7.60–7.76 (m, 4H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 13.98 (CH_3), 32.92 (CH_2), 123.12, 132.28, 133.84 (aryl), 168.21 (C=O).

3,3-Diethoxy-2-substituted-1-oxoisoindole **(3)***; general procedure*
EtOH (3ml) was added in one portion to a cold (–10 °C) suspention of **1** (5 mmol) in CH_2Cl_2 (30 ml) . The resulting clear solution was warmed to 23 °C over 20 min. Stirring with a solution of NaOH (2.00 g, 50 mmol) in H_2O (20 ml), extraction of the organic layer with CH_2Cl_2 (3 × 20 ml), drying over anhydrous Na_2SO_4 and evaporation of the solvent afforded a pale yellow oily product. Stirring under cold (–20 °C) petroleum ether (40–60), filtration and evaporation of the solvent gave the pure product.

3,3-Diethoxy-2-(4-methylphenyl)-1-oxoisoindole **(3a)**: From **1a** (2.96 g, 5 mmol) as described before. Yield: (1.41 g, 91%), m.p. 61–62 °C; pale yellow powder. IR (CH_2Cl_2): ν = 1594, 1636, 1731 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.22 (t, 6H, *J* = 7.3 Hz, $2CH_3$), 2.34 (s, 3H, CH_3), 3.26–3.38 (m, 4H, 2 CH_2), 7.17–7.78 (m, 8H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 14.93 (2 CH_3), 21.40 (CH_3), 57.54 ($2CH_2$), 102.11 (OCO), 120.38, 127.13, 128.11, 128.61, 129.77, 130.19, 132.60, 133.84, 135.21, 141.35 (aryl), 154.00 (C=O). Anal. Calcd for $C_{19}H_{21}NO_3$ (311.41): C, 73.37; H, 6.81; N, 4.50. Found: C, 73.11; H, 6.52; N, 4.33

2-Benzyl-3,3-diethoxy-1-oxoisoindole **(3b)**: From **1b** (2.96 g, 5 mmol) as described for **3a**. Yield: (1.45 g, 93%), pale yellow oil. IR (film): ν = 1614, 1713 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, 6H, *J* = 7.3 Hz, $2CH_3$), 2.81–2.95 (m, 4H, 2 CH_2), 4.57 (s, 2H, CH_2) 7.24–7.87 (m, 9H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 14.73 (2 CH_3), 41.74 (CH_2), 59.97 ($2CH_2$), 111.50 (OCO), 122.56, 123,79, 127.66, 128.59,129.71, 130.89, 132.74, 132.86, 138.05, 140.43 (aryl), 167.17 (C=O). Anal. Calcd for $C_{19}H_{21}NO_3$ (311.41): C, 73.37; H, 6.81; N, 4.50. Found: C, 73.21; H, 6.58; N, 4.21

2-Ethyl-3,3-diethoxy-1-oxoisoindole **(3c)**: From **1d** (2.65 g, 5 mmol) as described for **3a**. Yield: (1.11 g, 88%), pale yellow oil. IR (film): ν = 1614, 1713 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.21 (t, 6H, *J* = 7.2 Hz, $2CH_3$), 1.32 (t, 3H, *J* = 7.1 Hz, CH_3), 3.01–3.13 (m, 2H, CH_2), 3.11–3.23 (m, 2H, CH_2), 3.43 (q, 2H, *J* = 7.3 Hz, CH_2), 7.23–7.86 (m, 4H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 14.06 (CH_3), 15.07 ($2CH_3$), 32.90 (CH_2), 59.85 ($2CH_2$), 111.47 (OCO), 122.47, 123.52, 130.81, 132.48, 133.10, 140.37 (aryl), 167.02 (C=O). Anal. Calcd for $C_{14}H_{19}NO_3$ (249.34): C, 67.53; H, 7.69; N, 5.63. Found: C, 67.18; H, 7.33; N, 5.28

3,3-Diethoxy-2-propyl-1-oxoisoindole **(3d)**: From **1f** (2.72 g, 5 mmol) as described for **3a**. Yield: (1.18 g, 90%), m.p. 64–65 °C;

pale yellow fine crystals. IR (CH_2Cl_2): ν = 1611, 1713 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.00 (t, 3H, *J* = 7.1 Hz, CH_3), 1.18 (t, 6H, *J* = 7.2 Hz, $2CH_3$), 1.68–1.82 (m, 2H, CH_2), 3.00–3.22 (m, 4H, $2CH_2$), 3.33 (t, 2H, *J* = 7.1Hz, CH_2), 7.28–7.86 (m, 4H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 12.19 (CH_3), 15.11 ($2CH_3$), 22.25, 40.06 ($2CH_2$), 59.89 ($2CH_2$), 111.50 (OCO), 122.55, 123.62, 130.84, 132.52, 134.16, 140.36 (aryl), 167.25 (C=O). Anal. Calcd for $C_{15}H_{21}NO_3$ (263.37): C, 68.50; H, 8.05; N, 5.33. Found: C, 68.18; H, 8.23; N, 4.92

6-Chloro-2-ethyl-3,3-diethoxy-1-oxoisoindole (**3e**): From **1e** (2.82 g, 5 mmol) as described for **3a**. Yield: (1.23 g, 87%), pale yellow oil. IR (film): ν = 1611, 1716 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.16 (t, 6H, *J* = 7.3 Hz, $2CH_3$), 1.35 (t, 3H, *J* = 7.2 Hz, CH_3), 3.06–3.17 (m, 4H, $2CH_2$), 3.36 (q, 2H, *J* = 6.9 Hz, CH_2), 7.45 (d, 1H, *J* = 8.1 Hz, aryl-H), 7.55 (d,1H, *J* = 8.1Hz, aryl-H), 7.88 (s, 1H, aryl-H). ^{13}C NMR ($CDCl_3$): δ = 13.91 (CH_3), 15.02 ($2CH_3$), 33.12 (CH_2), 59.96 ($2CH_2$), 111.07 (OCO), 123.17, 123.86, 132.56, 134.84, 137.12, 138.56 (aryl), 165.52 (C=O). Anal. Calcd for $C_{14}H_{18}ClNO_3$ (283.78): C, 59.41; H, 6.41; N, 4.95. Found: C, 59.12; H, 6.28; N, 4.61

3-{1,1-Dimethyl-3-[chloro(N,N-dimethylamino)methylene] guanidine-2}-2-benzyl-1-oxoisoindolium hexachloroantimonate (**4a**): A solution of dimethylcyanamide (0.70 g, 10 mmol) in CH_2Cl_2 (20 ml) was added dropwise with stirring to a cold (–10 °C) suspension of **1b** (2.95 g, 5 mmol). The resulting clear solution was warmed to 23 °C over 30 min. The solvent is evaporated and the residue is crystallised at –20 °C from CH_3OH / Et_2O to afford faint yellow fine crystals. Yield: (2.05 g, 56%), IR (KBr): ν = 1590, 1675, 1766 cm^{-1}. ^1H NMR (CD_3CN): δ = 3.01, 3.17, 3.21, 3.38 (4s, 12H, 4 CH_3), 5.00 (s, 2H, CH_2), 7.31–7.42 (m, 5H, aryl-H), 7.75–7.98 (m, 4H, aryl-H). ^{13}C NMR (CD_3CN): δ = 39.69, 40.14, 42.22, 42.38 (4 CH_3), 43.72 (CH_2), 125.22, 125.72, 128.65, 128.88, 129.56, 130.31, 132.04, 135.34, 135.58, 137.18 (aryl), 149.74, 156.42, 161.67, 168.12 (C=N, C=O). Anal. Calcd for $C_{21}H_{23}Cl_7N_5OSb$ (731.38): C, 34.50; H, 3.17; N, 9.58. Found: C, 34.19; H, 2.83; N, 9.52.

3-{1,1-Dimethyl-3-[chloro(N,N-dimethylamino)methylene] guanidine-2}-2-ethyl-1-oxoisoindolium hexachloroantimonate (**4b**): From dimethylcyanamide (0.70 g, 10 mmol) and **1d** (2.65 g, 5 mmol) as described for **4a**. Yield: (2.17 g, 65%), IR (KBr): ν = 1588, 1681, 1770 cm^{-1}. ^1H NMR (CD_3CN): δ = 1.32 (t, 3H, *J* = 7.2 Hz, CH_3), 3.20, 3.43 (2s, 6H, 2 CH_3), 3.23 (s, 6H, $2CH_3$), 3.84 (q, 2H, *J* = 7.2 Hz, CH_2), 7.72–7.92 (m,, 4H, aryl). ^{13}C NMR (CD_3CN): δ = 14.09, 39.91, 40.22, 42.26, 42.44 (5 CH_3), 35.29 (CH_2), 124.89, 125.59, 130.44, 132.28, 135.09, 135.37 (aryl), 156.79, 162.08, 167.92, 172.69 (C=N, C=O). Anal. Calcd for $C_{16}H_{21}Cl_7N_5OSb$ (669.31): C, 28.72; H, 3.16; N, 10.47. Found: C, 28.43; H, 2.77; N, 10.12.

9-Methyl-11-substituted-5-oxoisoindolo[2,1-a]quinazolinium hexachloroantimonate **6**; *general procedure*

A suspension of **1a** (2.46 g, 5mmol) and appropriate nitrile (5mmol) in absolute dichloroethane (50ml) was boiled under reflux for 6 h. After cooling to room temperature, the solvent is removed under vaccum and the solid residue can be recrystallised from acetonitrile/ diethylether to give fine crystals.

9-Methyl-11-methylthio-5-oxoisoindolo[2,1-a]quinazolinium hexachloroantimonate (**6a**): From **1a** and methylthiocyanate (0.37 g, 5mmol) as described before. Yield: 1.63 g (52%)yellow fine crystals; m.p.260 °C (dec.). IR (KBr): ν = 1582, 1613, 1798 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 2.56 (s, 3H, CH_3), 2.71 (s, 3H, SCH_3), 7.59–8.08 (m, 7H, aryl-H). ^{13}C NMR (DMSO-d_6): δ = 13.18, 22.20 (CH_3), 122.12, 123.31,128.08, 129.54,130.80, 131.08, 131.41, 135.11, 137.88, 13794, 139.41, 145.43 (aryl-C), 159.54, 170.79, 172.15 (C=O, C=N). Anal. Calcd for $C_{17}H_{13}Cl_6N_2OSSb$ (627.76): C, 32.52; H, 2.09; N, 4.46. Found: C, 32.17; H, 1.87; N, 4.11

9-Methyl-11-phenyl-5-oxoisoindolo[2,1-a]quinazolinium hexachloroantimonate (**6b**): From **1a** and benzonitrile (0.52 g, 5mmol) as described for **6a**. Yield: 2.10 g (64%) orange fine crystals; m.p. 286–288 °C (dec.). IR (KBr): ν = 1578, 1614, 1802 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 2.53 (s, 3H, CH_3), 7.63–8.11 (m, 12H, aryl-H). ^{13}C NMR (DMSO-d_6): δ = 22.39 (CH_3), 121.52, 126.24, 128.70, 129.04, 129.57. 129.63, 130.48, 130.89, 131.08, 131.17, 131.46, 134.98, 137.73, 138.69, 139.35, 149.83 (aryl-C), 160.78, 167.62, 170.74 (C=O, C=N). Anal. Calcd for $C_{22}H_{15}Cl_6N_2OSb$ (657.83): C, 40.17; H, 2.30; N, 4.26. Found: C, 39.87; H, 2.57; N, 4.18

9-Methyl-11-(2-methylphenyl)-5-oxoisoindolo[2,1a]quinazolinium hexachloroantimonate (**6c**): From **1a** and 2-methylbenzonitrile (0.58 g, 5mmol) as described for **6a**. Yield: 2.22 g (66%) orange fine crystals; m.p. 235-237 °C (dec.). IR (KBr): ν = 1575, 1615, 1795 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 2.22 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 7.51–8.03 (m, 11H, aryl-H). ^{13}C NMR (DMSO-d_6): δ = 20.43, 22.35 ($2CH_3$), 121.37, 126.24, 128.13, 128.53, 129.40, 129.58, 130.96, 131.15, 132.75, 134.52, 137.42, 137.59, 137.63, 139.23, 139.98, 149.46 (aryl-C), 162.24, 167.57, 169.11 (C=O, C=N). Anal. Calcd for $C_{23}H_{17}Cl_6N_2OSb$ (671.86): C, 41.12; H, 2.55; N, 4.17. Found: C, 40.76; H, 2.69; N, 4.04

9-Methyl-11-(4-methylphenyl)-5-oxoisoindolo[2,1-a]quinazolinium hexachloroantimonate (**6d**): From **1a** and 4-methylbenzonitrile (0.58 g, 5mmol) as described for **6a**. Yield: 2.39 g (71%) orange fine crystals; m.p. 230–232 °C (dec.). IR (KBr): ν = 1577, 1605, 1801 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 2.46 (s, 3H, CH_3), 2.53 (s, 3H, CH_3), 7.28–8.09 (m, 11H, aryl-H). ^{13}C NMR (DMSO-d_6): δ = 21.96, 22.38 ($2CH_3$), 121.50, 126.31, 128.75, 129.58, 129.83, 129.93, 130.16, 130.43, 131.11, 131.41, 134.73, 135.03, 137.58, 138.79, 139.17, 149.92 (aryl-C), 160.78, 167.50, 170.77 (C=O, C=N). Anal. Calcd for $C_{23}H_{17}Cl_6N_2OSb$ (671.86): C, 41.12; H, 2.55; N, 4.17. Found: C, 40.81; H, 2.71; N, 3.89

9-Methyl-11-(1-naphthyl)-5-oxoisoindolo[2,1-a]quinazolinium hexachloroantimonate (**6e**): From **1a** and 1-naphthonitrile (0.77 g, 5mmol) as described for **6a**. Yield: 3.12 g (88%) dark brown fine crystals; m.p. 250–252 °C (dec.). IR (KBr): ν = 1576, 1613, 1795 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 2.58 (s, 3H, CH_3), 7.51–8.22 (m, 14H, aryl-H). ^{13}C NMR (DMSO-d_6): δ = 22.43 (CH_3), 121.77, 126.46, 126.50, 127.71, 128.31, 128.43, 128.89, 129.05, 129.14, 129.52, 129.64, 130.07, 131.13, 131.37, 131.80, 135.37, 137.21, 138.10, 138.91, 139.72, 149.19 (aryl-C), 161.35, 168.09, 168.86 (C=O, C=N). Anal. Calcd for $C_{26}H_{17}Cl_6N_2OSb$ (707.90): C, 44.11; H, 2.42; N, 3.96. Found: C, 43.83; H, 2.88; N, 3.59

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