CARBENE-FUNCTIONALIZED COMPOSITE MATERIALS

RELATED APPLICATIONS

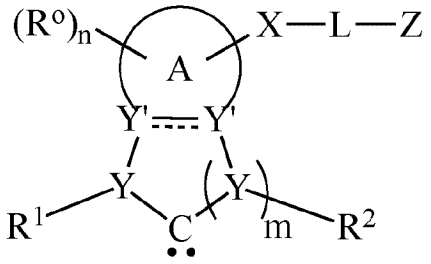
[redacted]

61/867,466, filed on August 19, 2013, and U.S. Provisional Patent Application No. 62/018,782, filed on June 30, 2014.

FIELD OF THE INVENTION

[redacted]

Organometallics **30**, 6713 (2011)], and NHC-based cross-coupling catalysts [E. A. B



(I)

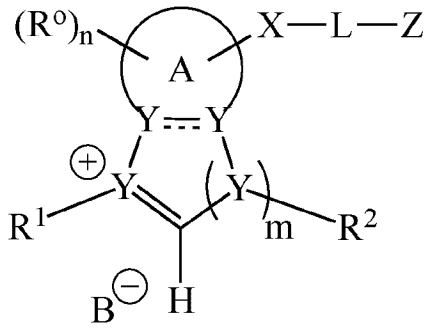
m is an integer from 0 to 4;

each R^o is independently H, halogen, the substituent X-L-Z as defined above, C_1-C_{10} alkyl, C_{10}-C_{20} alkyl, C_1-C_{10} alkenyl, C_{10}-C_{20} alkenyl, C_1-C_{10} alkynyl, or C_{10}-C_{20} alkynyl,

Y^2 and Y^3 are independently C or a heteroatom, and the dashed line represents an

optional double bond;

R^1 and R^2 are independently absent, at least one lone pair of electrons, H, C, O,



(II)

wherein:

n is an integer from 1 to 8, or from 1 to 4;

m is an integer from 0 to 4;

B is a counter ion that optionally acts as a base;

A is absent, an aliphatic cycle, a heterocycle, an aromatic ring, a fused aromatic ring

conjugated diene, thiol, or thioester, each of which is optionally substituted;

wherein:

m is an integer from 0 to 4;

D is a counterion that optionally acts as a base;

each Y is independently C or a heteroatom;

Y^2 and Y^3 are independently C or a heteroatom, and the dashed line is an optional

wherein:

n is an integer from 1 to 4, or alternatively 1 to 8;

m is an integer from 0 to 4;

G is a perhalogenated alkyl, perhalogenated alkenyl, perhalogenated alkynyl, a perhalogenated aryl, or OR', wherein R' is an aliphatic group, for example, an alkyl group.

A is absent, an aliphatic cycle, a heterocycle, an aromatic ring, a fused aromatic ring

[redacted]

optional double bond;

[redacted]

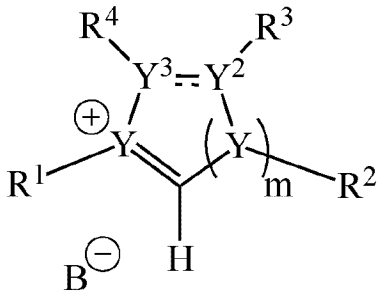
material forms at least part of an orthopedic instrument. In another embodiment, the metal

alkyl, C_{10}-C_{20} alkenyl, C_{10}-C_{20} alkynyl, C_{10}-C_{20} alkoxyl, C_6-C_{20} cyclic aliphatic moiety,

R^1 and R^2 are independently absent, at least one lone pair of electrons, H, C_{10}-C_{20}

m is an integer from 0 to 4;

In accordance with another embodiment, the carbene precursor is of formula Va



(Va)

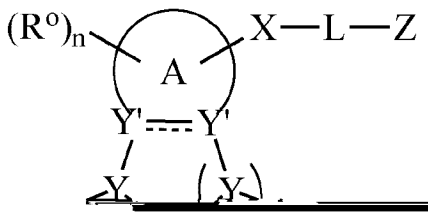
wherein:

m is an integer from 0 to 4;

B is a counter ion that optionally acts as a base;

each Y is independently C or a heteroatom;

Y^2 and Y^3 are independently C or a heteroatom, and the dashed line is an optional



G

(VI)

wherein:

m is an integer from 0 to 4;

each R^o is independently H, halogen, the substituent X-L-Z as defined above, C_{10}-C_{20} alkyl, C_{10}-C_{20} alkenyl, C_{10}-C_{20} alkynyl, C_{10}-C_{20} alkoxyl, C_6-C_{20} cyclic aliphatic moiety, aryl, ether, thioether, polyether, or polythioether, each of which is optionally substituted; or two of R^o together with the atoms to which they are attached are connected to form a cycle which is optionally substituted; and

optional double bond;

Table 3 presents results of stability tests of a representative NHC on Au(111). For most of

these XPS spectra, there is a high degree of overlap, suggesting no change following

our exposure to the stated conditions. In the C(1s) spectra on the last line, the upper spectrum

Figure 2B depicts an STM image of the monolayer prepared from the carbonate salt of [redacted] on Au(111) demonstrating highly ordered self assembly. A repeating lattice unit 2.65 [redacted]

Figure 3D depicts representative XPS data for the treatment of dodecanethiol–protected Au(111) surfaces with solutions of NHC-**1** for 24 h at room temperature; the XPS spectra

[redacted]

[redacted]

[redacted]

Figure 17A depicts SPR data from a commercial HPA chip in PBS buffer;

Figure 17B depicts SPR data from a NHC-**16** carbene chip in PBS buffer;

[redacted]

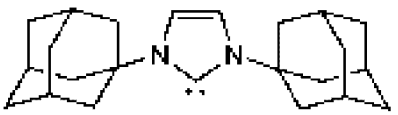
[redacted]

bond which can be unsubstituted or optionally substituted with one or more substituents

not limited to pyridinyl, pyrimidinyl, thiazolyl, pyridyl, dioxidothiomorpholinyl, dioxidothiazinyl, pyrazolidinyl

azetidinyl, azetidinonyl, oxetanyl, thietanyl, piperidinyl, piperazinyl, morpholinyl, pyrrolyl

pyrazinyl, thiazinyl, diazinyl, triazinyl, tetrazinyl, imidazolyl, benzimidazolyl, tetrazolyl, indolyl



As would be well appreciated by a worker skilled in the art, there are many alternative

retains its useful properties on the timescale of its expected usefulness in the presence of

air, moisture or heat, and under the expected conditions of application. This chemical stability may be defined relative to other self-assembled monolayer-functionalized surfaces

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

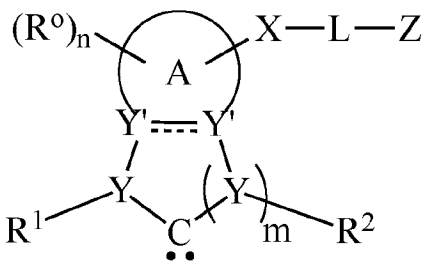
[redacted]

[redacted]

[redacted]

[redacted]

more carbenes of formula I



(I)

n is an integer from 1 to 8, or from 1 to 4;

conjugated diene, thiol, or thioester, each of which is optionally substituted;

optional double bond;

(II)

wherein:

n is an integer from 1 to 8, or from 1 to 4;

m is an integer from 0 to 4;

connected to form a cycle, or heterocycle, each of which is optionally substituted; and

R^1 and R^2 are independently absent, at least one lone pair of electrons, H, C_1-C_{10}

alkyl, C_{10}-C_{20} alkyl, C_1-C_{10} alkenyl, C_{10}-C_{20} alkenyl, C_1-C_{10} alkynyl, C_{10}-C_{20} alkynyl), cycloalkyl, aryl, heteroaryl, ether, thiol, thioether, amine, polyamine, polyether, polythioether, or polythiol, each of which is optionally substituted;

Formula II, C_1-C_{10} alkyl, C_{10}-C_{20} alkyl, C_1-C_{10} alkenyl, C_{10}-C_{20} alkenyl, C_1-C_{10} alkynyl,

which is optionally substituted;

optionally substituted;

polyether, or polythioether, each of which is optionally substituted; or, any one of R^3 or R^4 with any one of R^1 or R^2, together with the atoms to which they are attached

reagent or combination of reagents, or by displacing existing chemical groups or moieties

G.M. Whitesides, R.G. Nuzzo, *J. Am. Chem. Soc.* **111**, 321 (1989)]. The alkanethiol spontaneously forms a continuous, ordered, single-layer of the alkanethiol at the surface

an Au-S bond can be a poor conductor where compared to certain Au-C bonding

configurations [J.M. Cerqueira, *et al.*, J. Am. Chem. Soc. **132**, 5616 (2021)], coupling a

hydrocarbon-based compound to a metal via a carbon-metal bond, particularly one adjacent

thiols, remained, however.

ordered NHC film was inferred from NEXAFS C K-edge spectroscopy, but no stability studies were performed and no potential for derivatization illustrated. With respect to

prepared as a mixture of concentrated nitric and hydrochloric acid (1:3 ratio v/v). Gold wire was dissolved in an appropriate volume of aqua regia solution such that no solid remained.

iridium tips were used for all experiments. GXSM [Zahl, P., *et al. J. Vac. Sci. Tech. B* 28, C4E39 (2010)] was used as control software using the Signal Ranger A810 DSP and Nanonis HVA4 high-voltage amplifier.

To a solution of 4-amino-2-nitrophenol (616 mg, 4 mmol) and 1,12-dibromo

dodecane (2.624 g, 8 mmol) in anhydrous acetonitrile (40 mL), potassium carbonate (552

mg, 4 mmol) was added. The mixture was stirred at 80 °C for 8 h under argon. The solvent

into 25 mL of a saturated solution of $NaHCO_3$ in water and centrifuged. The desired product

was extracted from precipitate with $CHCl_3$ (3 x 25 mL). Yield 237 mg (69 %). ES-MS (m/z) for $C_{19}H_{30}N_6O$: 343.2387. Calc.: 343.2372. ^1H NMR (DMSO-d_6) δ (ppm): 8.06 (s, 1H, N-

C*H*=N), 7.44 (d, 1H, J_{HH} = 8.5 Hz, Ar*H*), 7.05 (s, 1H, Ar*H*), 6.78 (d, 1H, J_{HH} = 7.9 Hz, Ar*H*), 3.95 (t, 2H, J_{HH} = 6.5 Hz, -O-CH_2), 3.28(m, 2H, J_{HH} = 6.8 Hz, N_3-CH_2), 1.70 (m, 2H), 1.50 (m, 2H), 1.41 (m, br, 2H), 1.23 (m, br, 14H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ (ppm): 154.88 (s, N-CH=N), 141.39 (s, C), 137.78 (s, C), 133.45 (s, C), 116.27 (s, Ar), 111.75 (s, Ar), 98.19 (s, Ar)

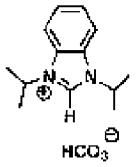
functionalization.

EXAMPLE 1D. Four step synthesis of 5-(dodecyloxy)-1,3-diisopropyl-1H-benzo[d]imidazol-3-ium hydrogen carbonate (NHC-1 hydrogen carbonate salt):

(i) 4-(dodecyloxy)-2-nitroaniline:

(iii) 5-(dodecyloxy)-1,3-diisopropyl-1H-benzo[d]imidazol-3-ium iodide:

EXAMPLE 1E. General Experimental Protocol for benizimidazole carbonate synthesis



Preparation of [iPr-BIMY(H)][HCO3] ("carbonate salt of NHC-1"):

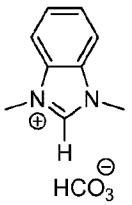
[redacted]

A similar procedure to Taton, Fèvre, M. *et al. J. Am. Chem. Soc.* **2012**, 134 (15)

[redacted]

6776-6784 and Fèvre, M. *et al. J. Org. Chem.* **2013**, 77 (22), 10135-10144 was followed

[redacted]



Each carbene was found to react with Au surfaces after simple room temperature immersion

of Au(111) or Au nanoparticles in a solution of the carbene or the corresponding carbonate

demonstrating thermal and oxidative stability. A large fraction of the surface even remained

[redacted]

EXAMPLE 5. NANOPARTICLES STUDIES

EXAMPLE 5A. Preparation of Gold Nanoparticles

Chloroauric acid tetrahydrate 50 mg, 0.126 mmol of in water (5.4 mL) was added to a solution of tetraoctylammonium bromide (167 mg, 0.306 mmol) in toluene (3.06 mL). The resulting mixture was stirred vigorously until the aqueous layer became colourless. Following

mixture was stirred vigorously for 20 min. 0.5 mM of dodecyl sulfide was added to the

a method described below. Resulting lattice constant was 4.107 Å, which is in good

to gold via three-fold hollow (tetrahedral) sites [H. Häkkinen, *Nature Chem.* **4**, 443 (2012)], with a reported binding energy of 127 kJ/mol [D. J. Lavrich, *et al. J. Phys. Chem. B* **102**,

(Figures 2A and 2B) showed no evidence of islands. However, islands were clearly present

in the STM image of NUC-2 on Au(111) (see Figure 5). The density of darker regions was

EXAMPLE 9. SPR EXPERIMENTS WITH NHC-16 AND COMPARISON TO COMMERCIAL "HPA" CHIP

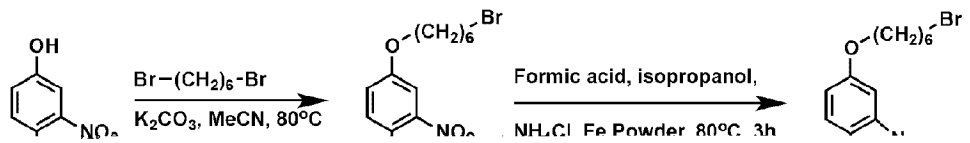
A Surface Plasmon Resonance (SPR) chip was prepared by depositing a NHC-**16** self-assembled monolayer on a blank Au chip (blank Au available from Biacore, General Electric, Pittsburgh, PA, USA). The resulting chip was consequently coated with a

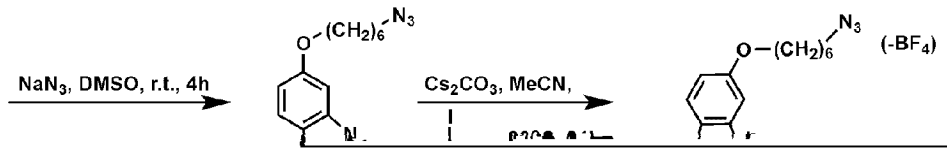
[redacted]

wide range of pH conditions that the carbone chip outperforms the commercial HPA chip in

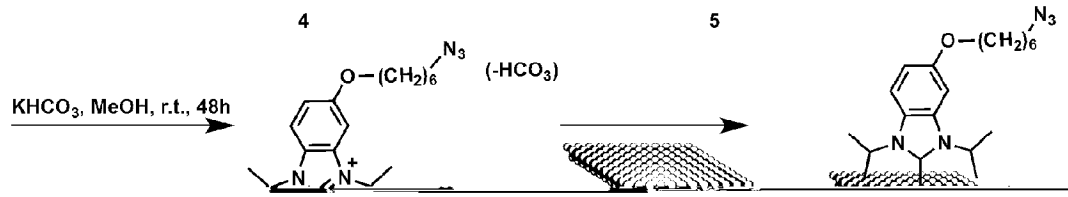
several ways: first, the magnitude of the reduction in phosphatidylcholine loading after the

Scheme 1:


OH
Br−(CH2)6-Br
K2CO3, MeCN, 80°C
O-(CH2)6-Br
Formic acid, isopropanol,
NH4Cl, Fe Powder, 80°C, 3h
O-(CH2)6-Br


NaN3, DMSO, r.t., 4h
O-(CH2)6-N3
Cs2CO3, MeCN,
O-(CH2)6-N3
(-BF4)

4 5


KHCO3, MeOH, r.t., 48h
O-(CH2)6-N3
(-HCO3)
O-(CH2)6-N3

[redacted]

K_2CO_3 (1.383g, 10 mmol) in a dry round bottom flask under Ar(g). 30 mL of dry acetonitrile

[redacted]

was added to the flask and the mixture was stirred until all of compound 1 had dissolved. 2

(dd, J = 8.7, 2.3 Hz, 1H), 7.11 (d, J = 2.1 Hz, 1H), 7.56 (d, J = 8.9 Hz, 1H), 8.02 (s, 1H)

Compound **5** was made by taking 0.388g of **4** (1.5 mmol) and 0.4887g of Cs_2CO_3

NHC-**9** was made by placing diphenyliodonium tetrafloroborate salt (0.037g) and CuSO$_4$ (0.8 mg, 5 mol%) in a vial and dissolving them in 2 mL of dimethylformamide (DMF).

[redacted]

NHC-**8** was then added to the solution and the vial was sealed with a TEFLON® cap. The

EXAMPLE 12. WATER OXIDATION STUDIES USING CERIUM AMMONIUM NITRATE AND UV ABSORBANCE DETECTION

These experiments are intended to demonstrate that NHC-terminated metal complexes

are capable of oxidizing water. A sacrificial oxidant, cerium ammonium nitrate ("CAN"), was used both to complete the oxidation cycle and to track the progress of reaction by monitoring

100 °C or 120 °C for 24 h. After this time, the samples were cooled to room temperature

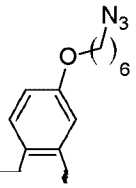
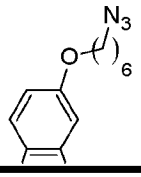
rinsed with benzene (3 x 5 mL), ether (3 x 5 mL), and ethanol (3 x 5 mL), dried under a

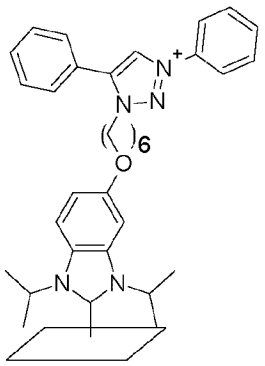
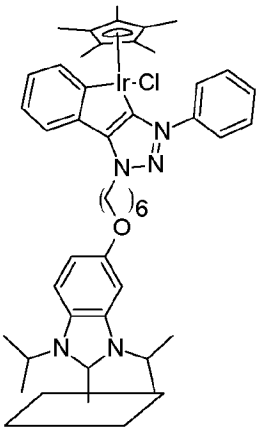
nitrogen gas stream, and analysed by XPS. The samples treated at 100°C showed no discernible change, while the samples treated at 120°C showed decomposition (see Figures

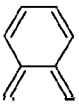
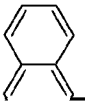
TABLE 1: Structural information for NHCs on metal.

Nickname	Structure	Name of NHC/salt	Prepared from

		1,3-bis(2,4,6-	

NHC-7		5-(6-azidohexyloxy)-1,3-diisopropyl-2,3-dihydro-1H-[illegible]	

NHC-9			
NHC-10			

Monolayer prep'd using [redacted]		1,3-diisopropyl-naphtho[2,3-d]imidazolium	

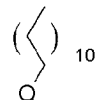
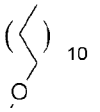
Monolayer		5-(dodecyloxy)-1,3-	

TABLE 2A: XPS data for products obtained by reacting NHCs with Au(111) surfaces and Au nanoparticles

Carbene NHC on GOLD	N:C ratio (XPS)		
	Expected	Found	
		Au(111)	Au_{NP}
NHC-**1**	2:13	2:14	2:13
NHC-**2**	3:20	3:21	3:22

TABLE 3: Stability Tests of Self-Assembled Monolayers: Films of NHC-1 deposited on Au(111) from its hydrogen carbonate precursor before and after exposure to listed conditions.

Conditions	N(1s) Spectra	C(1s) Spectra

	— Starting — H2O, 100°C, 24h	— Starting

TABLE 4: Characterization of NHC-1-substituted Pd nanoparticles.

Pd		Stabilizing			

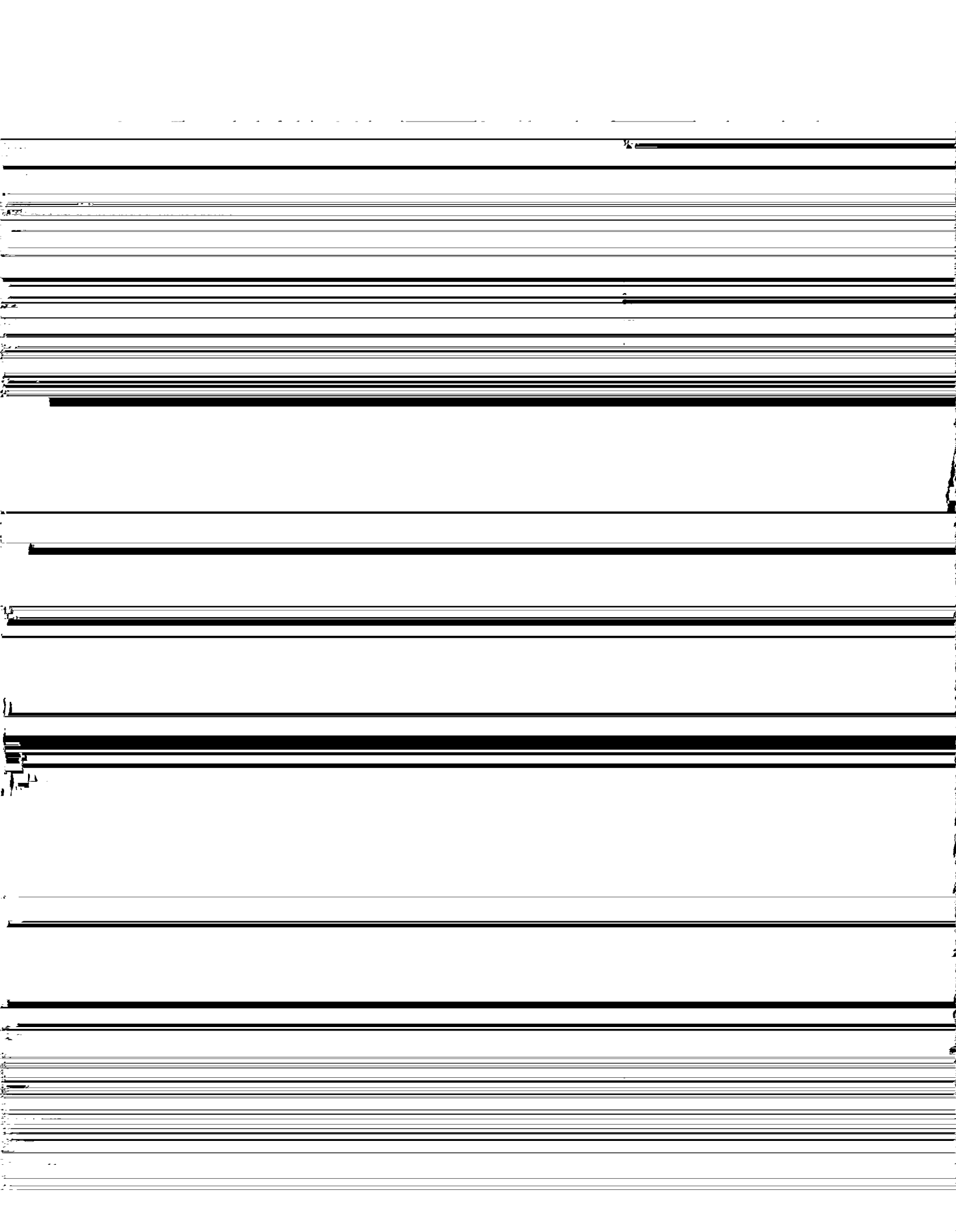
			804±33	563±40	516±40	212±13

All publications, patents and patent applications mentioned herein are indicative of the level of skill of those skilled in the art to which this invention pertains.

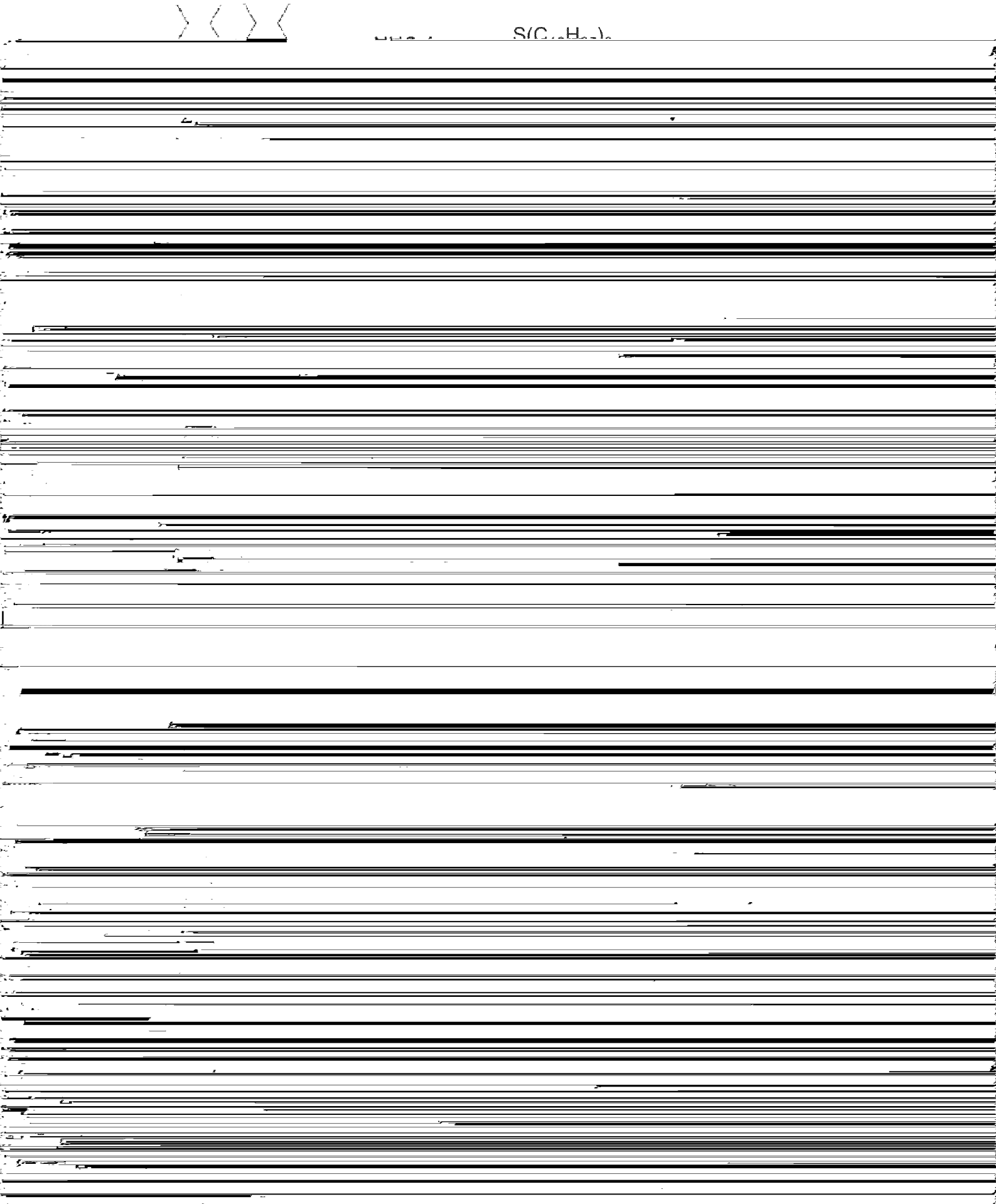
[redacted]

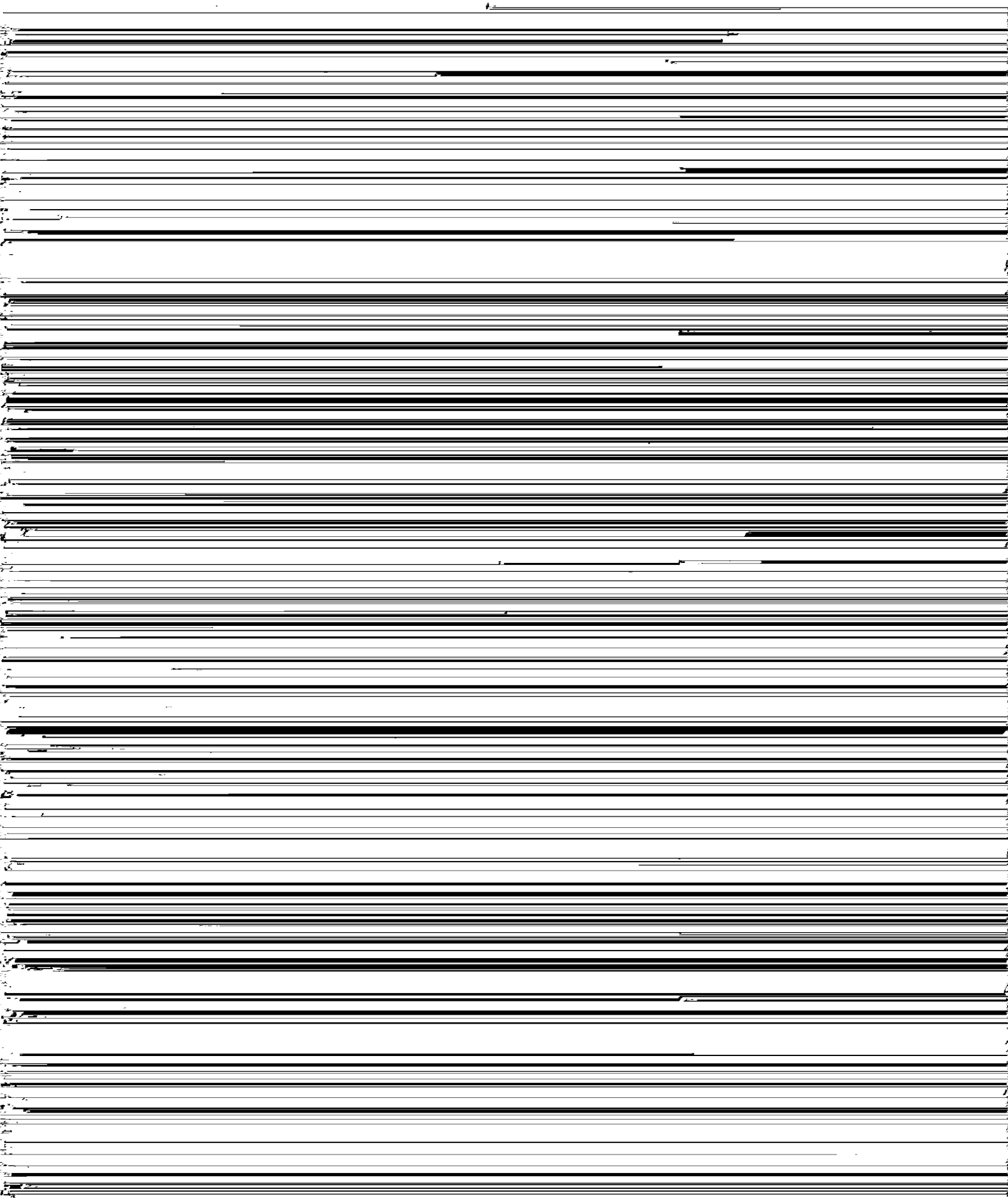
many ways. Such variations are not to be regarded as a departure from the spirit and scope of [redacted]

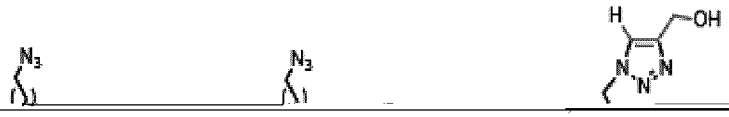
1,3-dihydro-1,3-bisisopropyl-2*H*-benzimidazol-2-ylidene

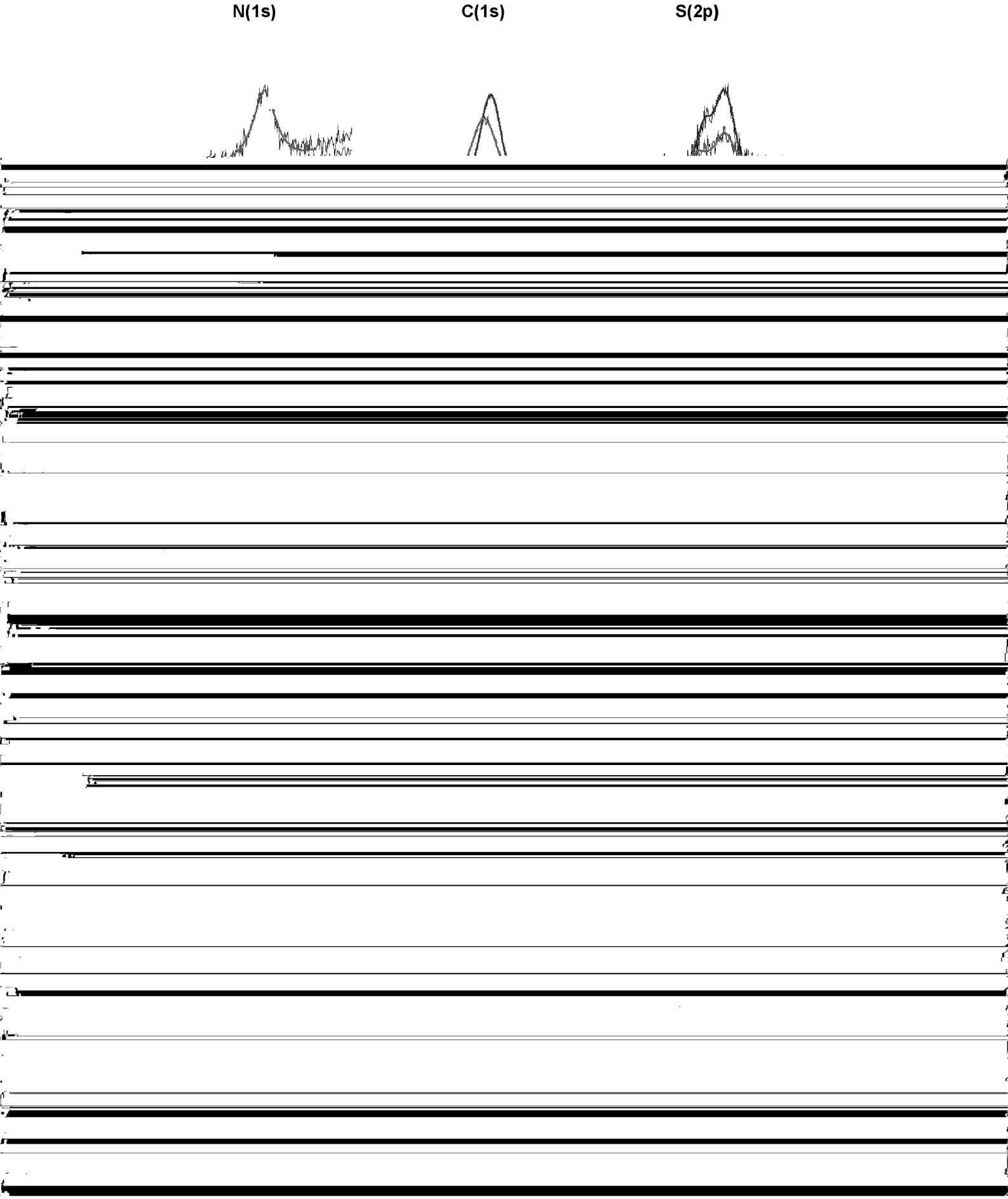


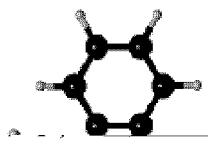
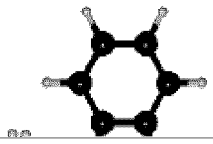
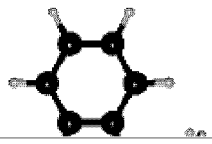
15. Use of the carbene-functionalized composite of any one of claims 1 – 6 or of the carbene-functionalized composite prepared by the method of any one of claims 7-13 for:

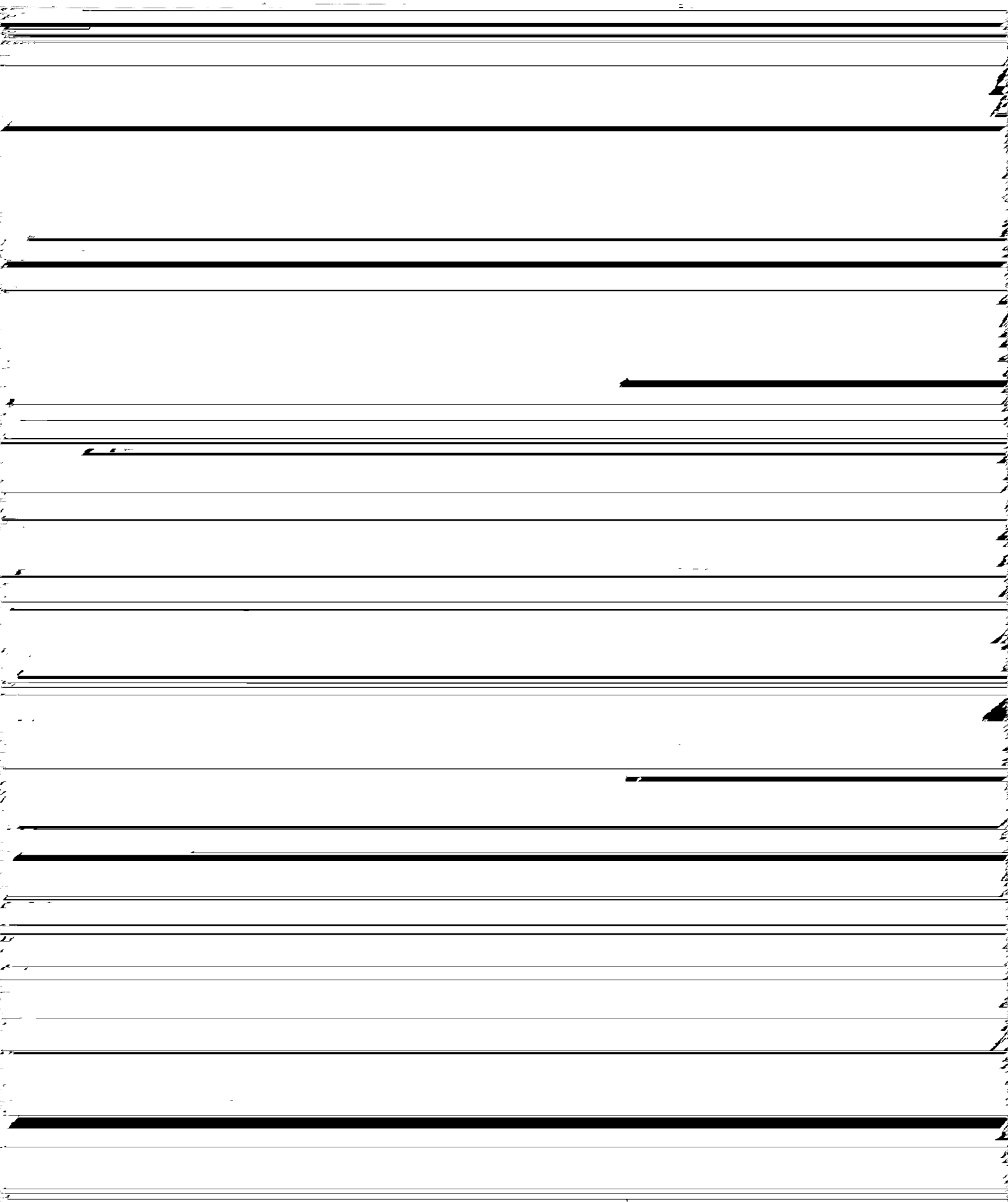



N(1s)
C(1s)
S(2p)

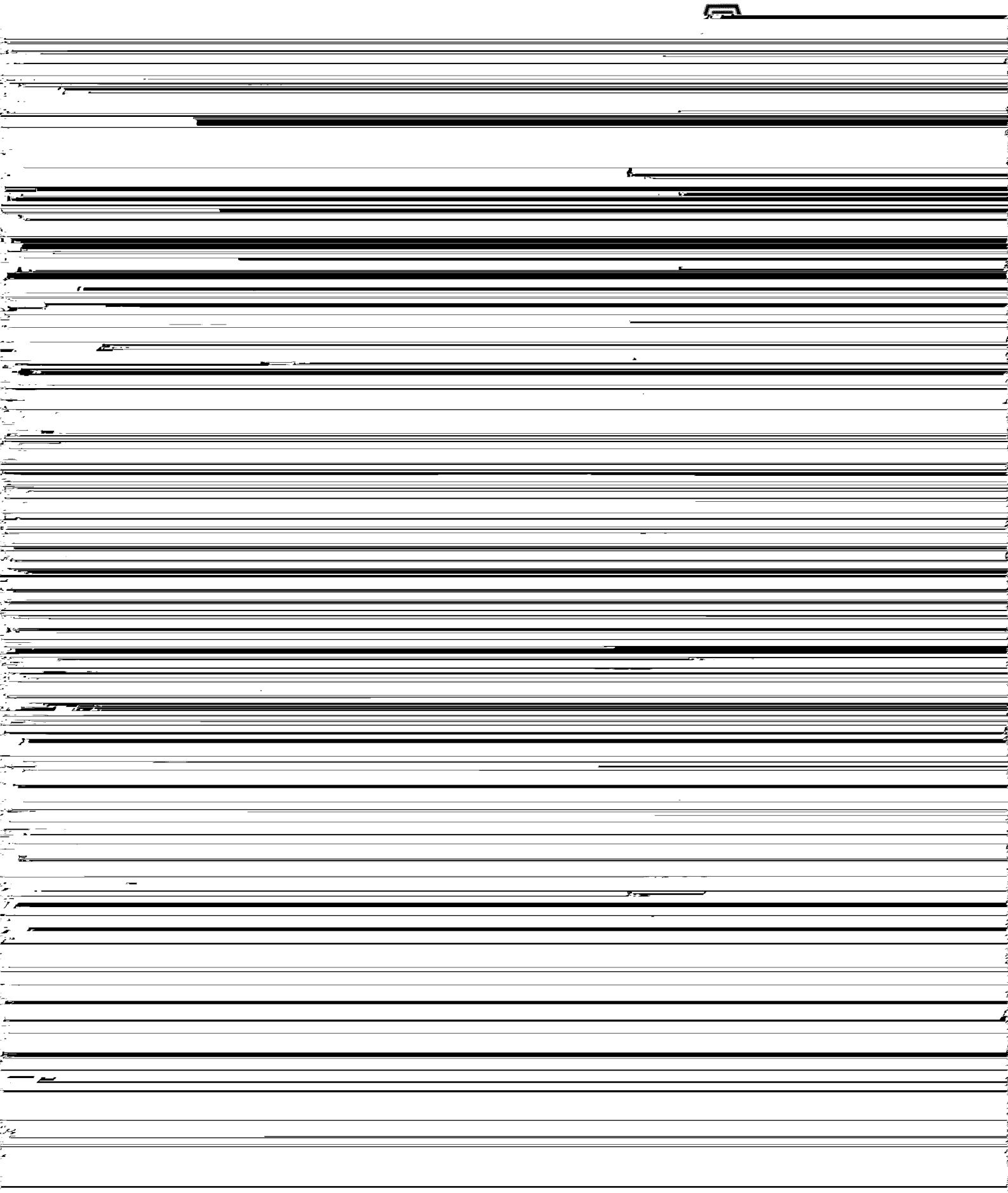


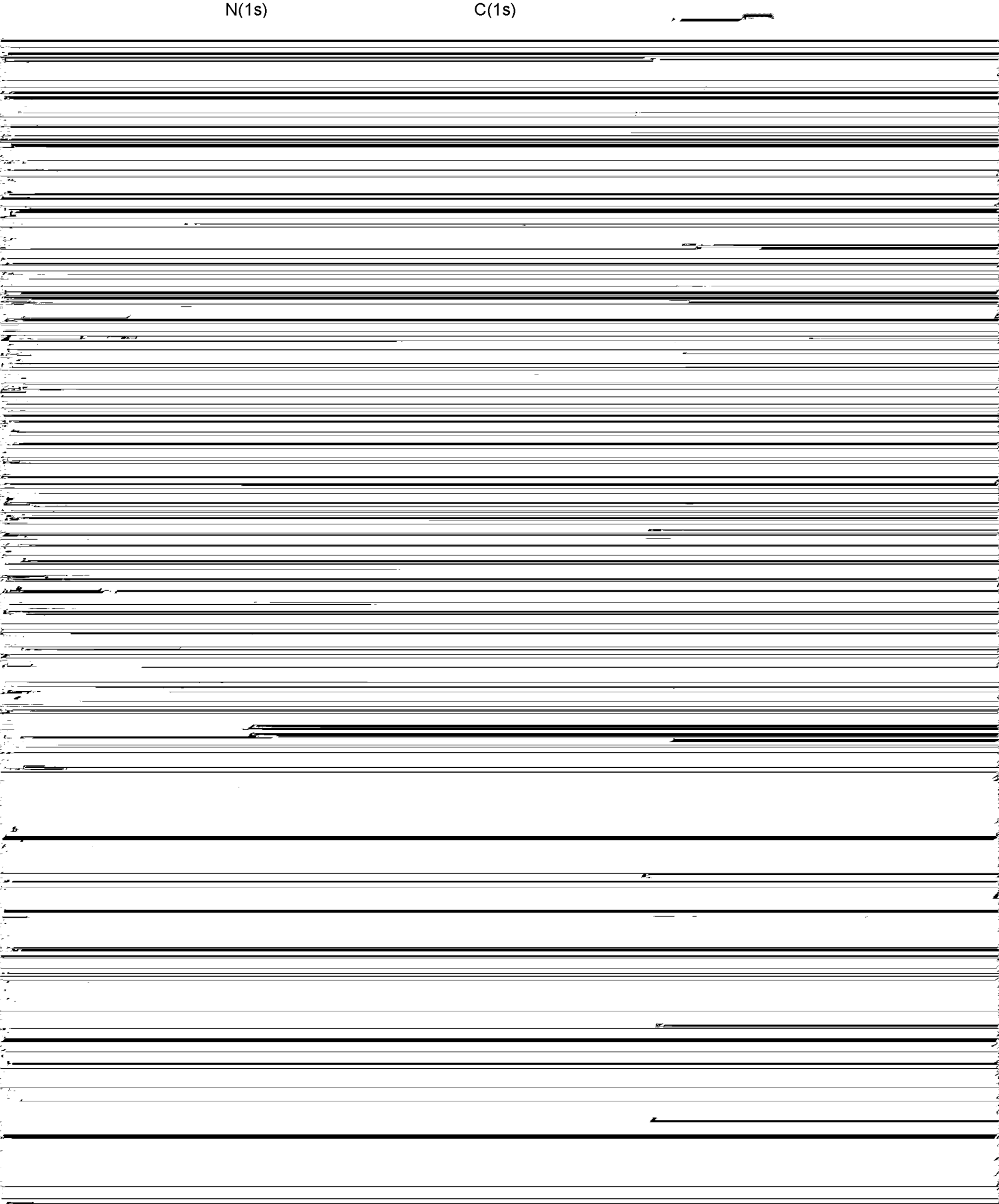

N(1s)
C(1s)
S(2p)

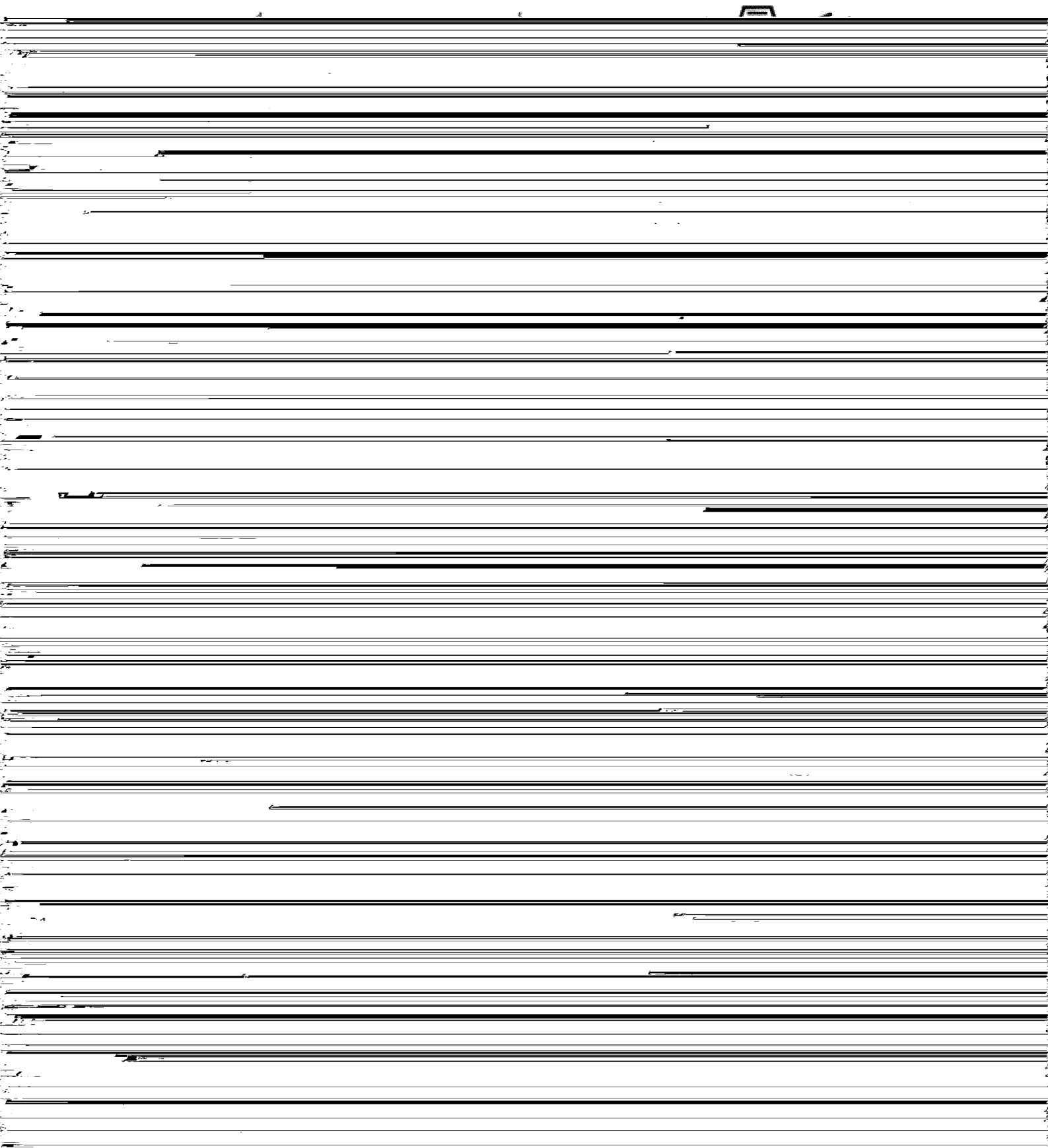




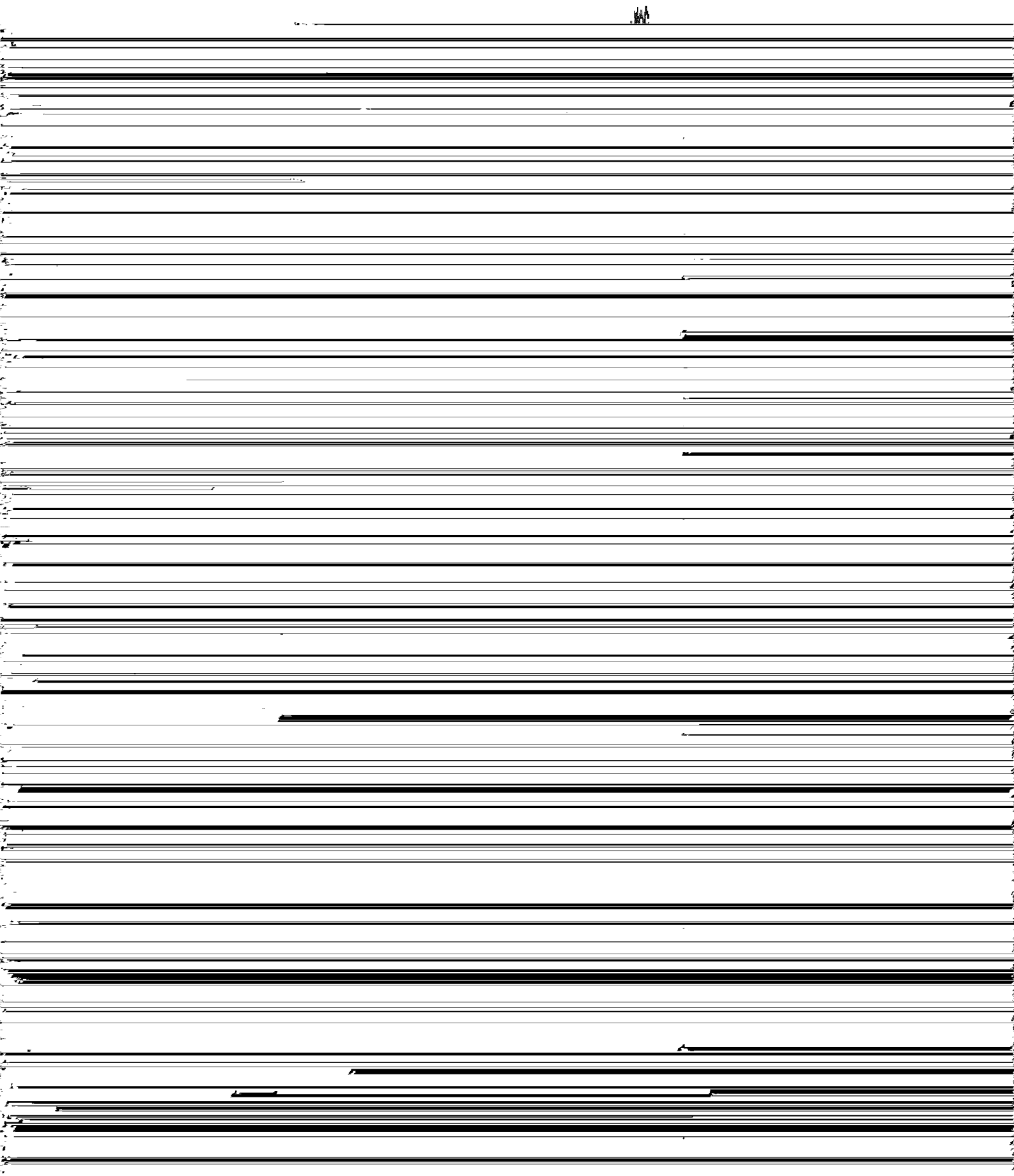



N(1s)
C(1s)
Ph
N
N
N

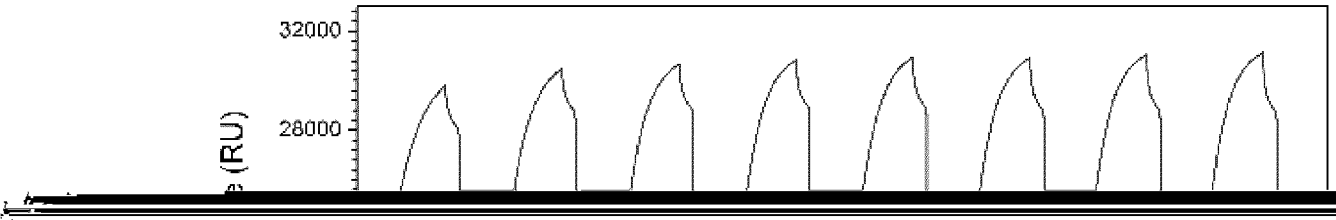


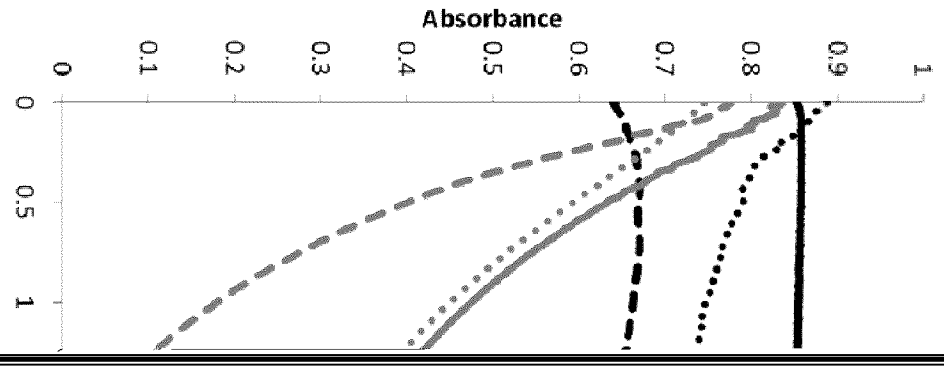

N(1s)
C(1s)


N(1s)
C(1s)


N 1s
C 1s


24000


32000
28000
(RU)


Absorbance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
0.5
1

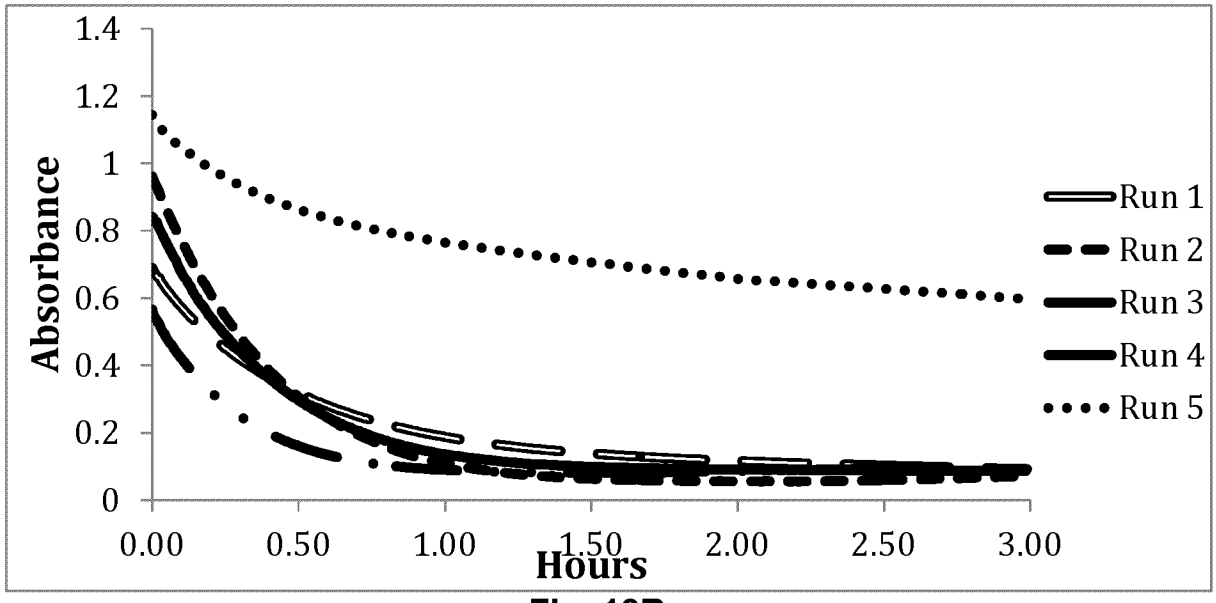
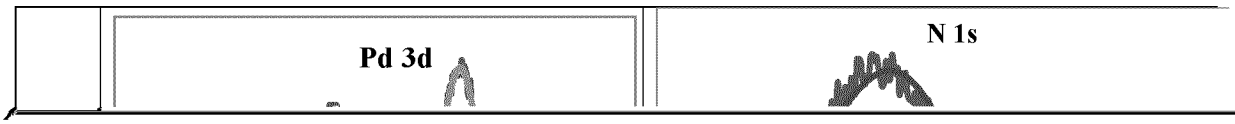

1.4
1.2
1
0.8
0.6
0.4
0.2
0
Absorbance
0.00
0.50
1.00
1.50
2.00
2.50
3.00
Hours
Run 1
Run 2
Run 3
Run 4
Run 5

Fig. 18B


Pd 3d
N 1s


Starting
Starting

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 February 2015 (26.02.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/024120 A1

(51) International Patent Classification:
B32B 15/04 (2006.01) *G01N 21/77* (2006.01)

(74) Agents: OSLER, HOSKIN & HARCOURT LLP et al.; Suite 1900, 340 Albert Street, Ottawa, Ontario K1R 7Y6

(21) International Application Number:
PCT/CA2014/050794

(22) International Filing Date:
19 August 2014 (19.08.2014)

(25) Filing Language: English

(26) Publication Language: English

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,