From Small Rings to Big Things: Xerography, Sensors, and the Squaraines

Brian Halton

School of Chemical & Physical Sciences, Victoria University, PO Box 600, Wellington
(e-mail: *brian.halton@vuw.ac.nz*)

The process that has become the modern miracle of photo-copying was discovered in 1938 by patent attorney Chester Carlson who had studied chemistry in college, but gained a BSc in physics. His patent was granted in November 1940 under the title *Electron Photography* (Fig. 1).[1] The term **xerography** (*xeros*: dry, *graphos*: writing) was coined subsequently because there were no liquids involved in the chemical process.[2,3] Without the *Xerox* life would be almost impossible, especially as it extends to laser (and LED) print-ers and copiers. It took Carlson years to stimulate interest in developing the potential of what he had found: it was only through the non-profit *Battelle Memorial Institute* of Ohio and an agreement in 1947 with the small Rochester photo-paper company *Haloid*, that the invention progressed to the first commercial office copier. The 914 copier, as it was known, appeared in 1959 and copied sheets 9 x 14 inches in size; Haloid has evolved into what we now know as the *Xerox Corporation*.

Fig. 1. Frontispiece of Carlson's patent (from http://www.freepa-tentsonline.com).

The basic principles of xerography are simple enough. First, a positive charge is applied to a photoconductive surface (the photoreceptor) and then the image of a document is exposed on this surface, which causes the charge to drain away from the surface in all but the dark image areas (these remain un-exposed and thus charged). Next, a negatively charged pow-der (a dry ink or toner) is cascaded over the surface so that it adheres to the positively charged parts and creates a visible image. By placing a sheet of positively charged plain paper over the image, the negatively charged powder is attracted to the paper electrostatically, transferring the image. Finally, the powder image is fused to the paper by heat and the photo-conductive surface cleaned ready for subsequent use.

Laser printing was also introduced by Xerox in the mid-1970s, but its true potential has been realised only with the advent of the personal computer, the internet and data trans-fer. In the modern machine the document is moved automati-cally from the document handler to a platen that is housed under it, scanned, and the data stored in the raster memory (a raster is a horizontal strip of dots across the page). From here the digitized image of a page is projected by the laser onto the charged photoreceptor belt to give the latent image as described above. More than >90% of the photoreceptors currently used are organic photoconducting materials.[3] Mag-netic rollers brush the belt with oppositely charged dry ink

and create the visible image by adhering to the latent im-age. As the copy paper moves from its storage tray towards the belt, it is charged to the same polarity as the belt and thus attracts the dry ink from it, so creating the image that is heated and pressed between two rollers to fuse the dry ink to the paper. The process is repeated until the entire document is printed. The original single layer device evolved to a bi-layer system, where the charge generation and charge trans-port functions are separated into two discrete layers. It is the availability of the organic photoreceptor that impacts most on xerographic copying. Various classes of organic photo-conductive pigments have been developed and successfully used in the bilayer device. These need to be insulators (or have low conductivity) in the dark but become conductors upon exposure to light.[3]

This is where small ring chemistry, inextricably linked to W. H. Perkin Jr. and the 1880s,[4] and all too often dispelled as mere chemical curiosity, comes into play. In 1959 (when the 914 copier was released) Cohen, Lacher and Park[5] reported a new cyclobutadienoacid derivative, the diketocyclobu-tenediol **1**, that was subsequently given the trivial name of *squaric acid*.[6] It is best prepared by complete hydrolysis of the tetrafluorodiether **2**. Because each carbon centre of **1** is sp[2] in nature, the molecule is exceptionally acidic (pK_a *ca.* 3.0) and exists entirely in the symmetrical dianionic *squa-rate* form $(C_4O_4)^{2-}$.
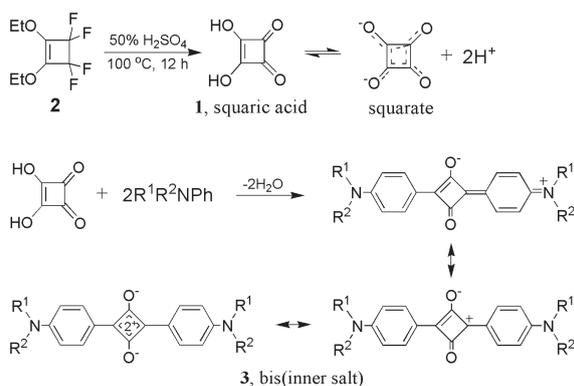
Scheme 1

Some three years later, the condensation of squaric acid with reactive pyrroles was recorded[7] prior to tertiary aromatic amines being employed in the reaction (Scheme 1).[8] The reaction products, illustrated by **3**, are highly conjugated and intensely coloured betaine (di-ionic) dyes with high melting points, as expected for polar molecules. They differ from earlier dyes because the salts are intramolecular (in-ner) rather than ion-paired with a dye base; they were named *squaraines*.[7] These derivatives absorb at long wavelength (620-670 nm in solution; 700-850 nm in the solid state) and fluoresce with reasonable quantum yield. Their excited state lifetimes mean that their photostabilities are good and pho-tosensitivity over the visible-near IR region is excellent. The

ground and excited singlet states (S_0 and S_1) of **3** are intermolecular donor-acceptor-donor (D-A-D) charge-transfer in nature, with the nitrogen atoms the donors and the central four-membered ring the acceptor. In the solid state the layers are *ca*. 35 nm apart (Fig. 2). Intramolecular charge-transfer occurs during $S_0{\rightarrow}S_1$ excitation, but this is largely (~80%) confined to the central C_2O_4 moiety.[9] The absorption characteristics and *intermolecular* charge-transfer of the squaraines form the basis of their use in diode laser printers, copiers, and multifunctional copier-printers. Initially, they were used as sensitizers for ZnO photoconductors,[10] but were recognised as bilayer photoconductors in 1974.[11] Because their absorption matches well to the diode laser, there was rapid development in the 1980s of their syntheses, and patents appeared for their composition and uses.[12] Fluorinated derivatives were patented for photoconducting imaging,[13] and studies on the structural and electronic properties[9] continue even now.[14] In 1993, the unsymmetrical fluorodiether **4** was recorded as the most outstanding squaraine known.[3]
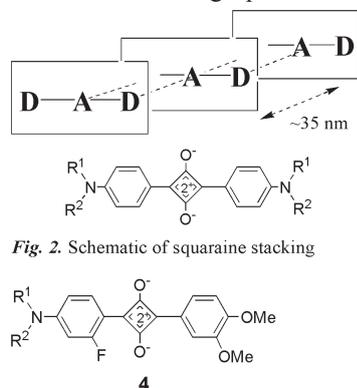

Fig. 2. Schematic of squaraine stacking

4

Despite these advances, it was found that residues from the squaric acid synthesis were carried through to the squaraines and that these reduced the efficiency of xerography by imposing low charge-acceptance and a high *dark-conductivity*. In 1986 Law and Bailey[15] removed these obstacles by providing derivatives from a route that avoided squaric acid itself (Scheme 2). The squaraines from this so-called *ester route* have a smaller particle size with different crystallographic orientation that gives rise to improved xerographic properties. Further development came from the same authors in 1990 from their use of the [2 + 2] addition of a ketene to an alkene (Scheme 3) that allowed for easy synthesis of unsymmetrical derivatives.[16]
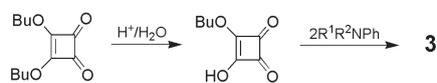

Scheme 2
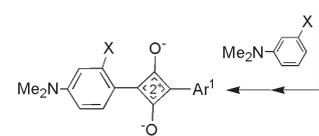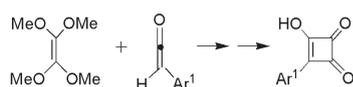
Ar^1 = 4-$MeOC_6H_4$- or 3,4-$(MeO)_2C_6H_3$-,
X = H, OH, Me, or F

Scheme 3

Of course, it is not just squaraines that are used as photoreceptors for xerography. Chart 1 depicts the important classes of compounds that are in use,[3] which include azo pigments such as **5** (known as CGM), perylenes (exemplified by bisamide **6**), and phthalocyanines **7** which may or may not have a co-ordinated metal.

Chart 1

5, CGM

6, a perylene dicarboxamide

7, a phthalocyanine,
M = metal or 2H
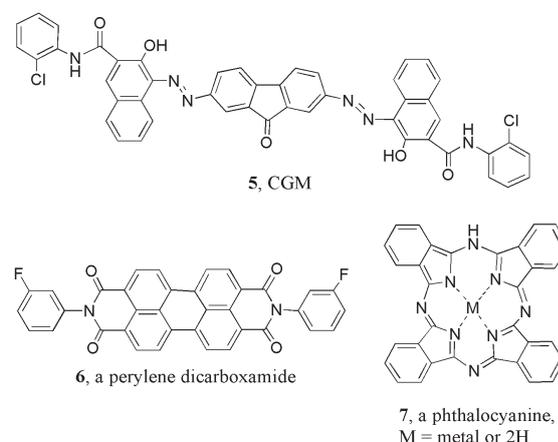
Since the squaraines are long wavelength-absorbing fluorescent materials with acceptable quantum yields, reasonably long excited state lifetimes, and good photostabilities, they have also found use in fluorescence-based assays.[17] The most suitable compounds for biological applications carry an indolenine derivative, *e.g.* **8** (Chart 2), as these have the highest photostabilities. Importantly, their use is further enhanced because quantum yields and lifetimes increase significantly upon covalent and noncovalent binding to proteins [bovine serum albumin (BSA), antibodies]. The absorption range allows use with the commercially available 635- and 650-nm diode lasers, and the detection limit for *e.g.* **9**, in blood was shown to be half that of an alternative commonly used fluorophore.[18] Even the simple phenolic squaraine **10** binds to BSA with a profound colour change in solution and in gel - pink to deep purple - and it is some five times more sensitive than dyes in common use.[19]

Chart 2

8, an indolininyl squaraine

9

10

11, bis(inner salt)

12, Cy5
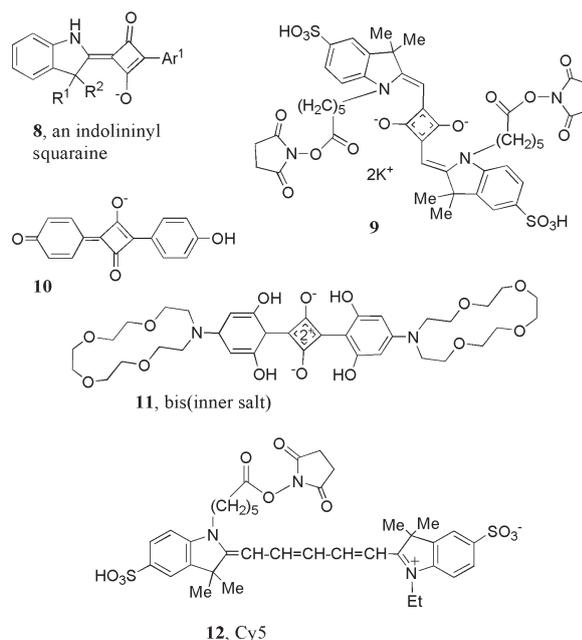
Fluoroionophores containing azacrown-substituted squaraines, *e.g.* **11**, have been used for Na^+ and K^+ sensing in plasticized PVC matrices and provide an alternative to use of flame emission spectroscopy.[20] A fluorescent squaraine-

containing chemosensor that signals change in the pH 7-10 range works in wholly aqueous solutions.[21] The electrophilic squaraine four-membered ring also has been used in aqueous solution for a highly selective colorimetric chemo-dosimeter for thiol-containing compounds; derivatives have been used successfully in the determination of low molecular mass aminothiols in human plasma.[22] Ring-substituted squaraines are at least as effective as the indolium dye Cy5 **12** that is a commonly used fluorescent label. As the squaraines are excited with both red and blue diode lasers or light emitting diodes, they can be used as fluorescent probes and labels for intensity- and fluorescence lifetime-based biomedical applications.[23] However, such uses for squaraines have been significantly limited by their chemical sensitivity to attack by strong biological nucleophiles and their ability to form non-fluorescent self-aggregates. The most recent advances have had a marked impact on both of these problems: specifically, encapsulation of the thread-like squaraine dye inside an interlocked pseudorotaxane structure adds very significant stability.[24] As an example, the molecular cage **13** complexes squaraine **14** and, in the presence of Na^+, gives the rotaxane **13⊂14⊃Na$_2$** as its perchlorate salt (Scheme 4). The Na^+ ions provide ion-specific binding to the encapsulated thread-like squaraine dye and the pseudorotaxane structure protects it from attack. Analogues with Zn(II)-dipicolylamine coordination centres, *e.g.* **15⊂16,** are formed from macrocycle **15** and **16** (Scheme 4).[25] Such pseudorataxanes are cell-targeting ligands with **15⊂16** having a photobleaching half-life 10 times greater than that of the Cy-5 analogue **17** (Chart 3). The rotaxane **15⊂16** $4NO_3^-$ is some 20 times more stable than Cy-5 and provides an extremely bright, highly stable near infrared (NIR) fluorescent probe for *in vitro* and *in vivo* optical imaging of live and fixed cells. Such derivatives seem set to be superior substitutes for Cy-5 in many biological applications.[25] Such stabilization has an analogy with amphiphilic squaraines (derivatives of **3** with ether, alcohol and carboxyl substituents) that interact efficiently with micelles with little change in their absorption characteristics.[26] Again, the squaraine is encapsulated and the fluorescence lifetime is more than doubled in Triton X-100, **18**. The encapsulated squaraine appears to sit close to the micelle surface near the polar head groups and, because micelles mimic biological media, applications are likely.

Pharmacologically acceptable derivatives of bromo- and iodo-derived squaraines **19** (Chart 3) find use as sensitizers in photodynamic therapy (PDT), an emerging procedure for diagnosis and treatment of cancer as it involves the inactivation of living cells.[27] After intravenous injection, the tumor tissues selectively retain the photoactive sensitizer (the squaraine) that liberates the highly reactive species upon exposure to specific NIR radiation. Cellular constituents are then damaged and eventually die. PDT is a safer treatment than conventional chemotherapy and radiotherapy, since the induction of cytotoxicity ceases when the light is switched off. The quinaldine-based squaraines, *e.g.* **20**, appear to have much potential here.[28]

By the mid-1990s the ability of squaraines such as the bis(trihydroxybenzene) derivative **21** to provide nanocrystalline semiconductor films with TiO_2, ZnO and SnO_2 colloids was recognised, and their possible use in sensitizing large bandgap semiconductors continues to be explored.[29]

Scheme 4

13

14, R = NEt$_2$

13⊂14⊃Na$_2$, R = NEt$_2$

15

16

15⊂16 $4NO_3^-$

Chart 3

17, Cy5 analogue

18, Triton X-100
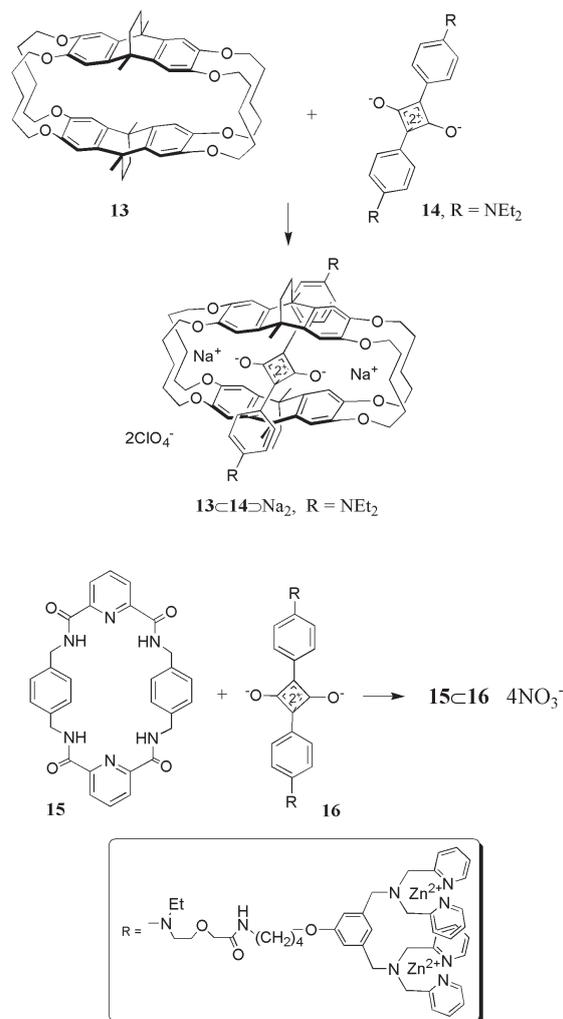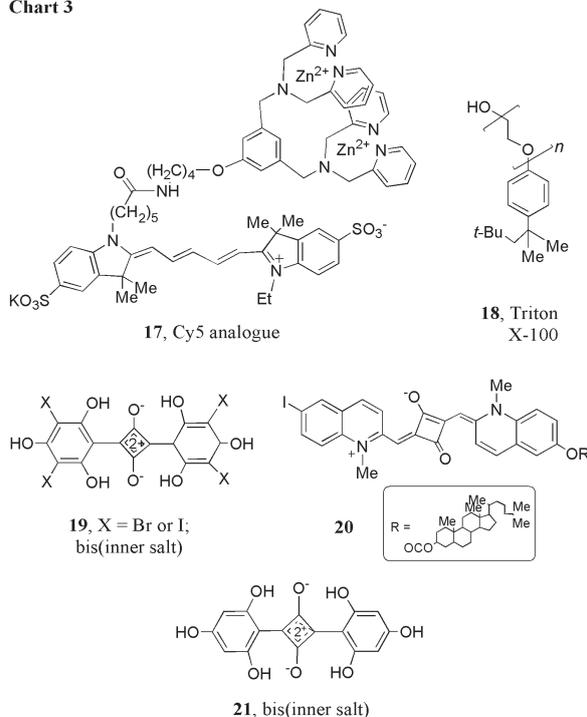
19, X = Br or I; bis(inner salt)

20

21, bis(inner salt)

Squaraine-containing non-linear optical (NLO) devices were patented over a decade ago[30] and NLO properties continue to receive attention. Derivatives with peripheral arylethene moieties, *e.g.* **22** (Chart 4), provide compounds whose independent components are separately represented in functional

Chart 4

22

23

24, R = Me or Bu
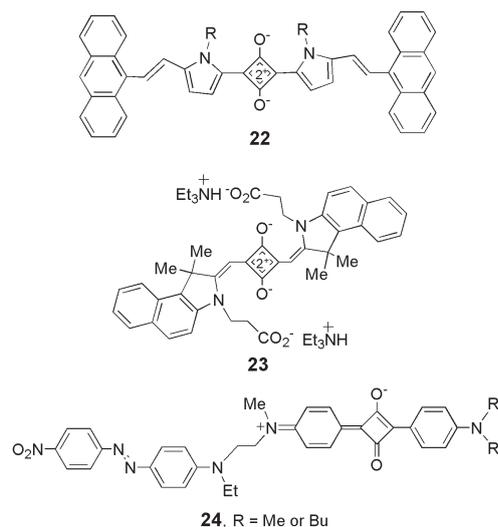
molecular materials.[31] Differently functionalized derivatives have electron-transporting properties, some with both electron- and hole-transporting ability. One such compound, when inserted between a cathode and an anode, gave a single-layer-sandwich device with red light-emitting ability under both low negative and low positive driven bias.[32]

The novel blue squaraine dye **23** carrying two carboxylate groups has been successfully used in liquid- and solid-state NIR dye-sensitised solar cells.[33] Furthermore, a squaraine chromophore attached to a podand chain gives proton-controlled, intramolecular photoinduced electron transfer (PET)[34] that has application in the design of PET-based sensors. Finally, the coupling of the squaraine moiety with the azo dye Disperse Red 1 gives the dark green **24** (Chart 4) which has the rare combination of fluorescent and azo units within the same molecule, providing a promising system for optical data storage.[35]

Cohen, Lacher, and Park[5] could hardly have envisaged the potential importance of their squaric acid and the uses to which the squaraines have been put. Further advances in squaraine usage can be expected for some little while yet. This account serves to emphasise once again that pure research is the necessary forerunner to so much applied and technological development.

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