Cover Essay

Cadet's Fuming Arsenical Liquid and the Cacodyl Compounds of Bunsen

Part I. Discovery by Cadet de Gassicourt and Work of Other Early French Chemists

Arsenic is a *metalloid*, not a metal, but organoarsenic compounds, like the organic compounds of the other metalloids, boron, silicon, germanium, and tellurium, following long-standing tradition going back to the 1850s and 1860s, are included in the "organometallic compound" classification. Indeed, an organoarsenic compound, tetramethyldiarsine ("cacodyl"), our cover molecule, played a vital role in the development of organometallic chemistry.

It was a French pharmacist-chemist, Louis-Claude de Gassicourt (1731−1799), who prepared the first organoarsenic compounds, although he did not know that he had done so. The experiment, carried out in 1757, that produced them was only indirectly related to the research that Cadet was doing at the time, the preparation of invisible inks by the action of various acids on arsenic-containing cobalt ores, $CoAs_2$ and $CoAsS_2$. The connection seems to be that the former is a source of arsenious oxide, As_2O_3, and that Cadet had developed an improved synthesis of potassium acetate. In any case, Cadet's famous experiment involved the thermally induced reaction of arsenious oxide with potassium acetate. It is interesting to hear about this experiment in his own words[1] (in free English translation):

> I take two ounces of arsenious oxide (confusingly called "arsenic" in those days), reduce it to a very fine powder in a marble pestle, add two ounces of thin plates of potassium acetate and place this mixture in a glass retort which then is placed in a small reverbatory furnace. The retort is connected to a glass receiver. I heat (the mixture) slowly. First a slightly colored liquid of an extremely penetrating garlic odor distills and then a red-brown liquid which fills the receiver with thick fumes.
>
> On continued distillation a black powder sublimes into the neck of the retort which looks like what the Germans call 'Mückengift' (fly poison); one finds also some arsenic metal and a material that burns like sulfur when exposed to the flame of a candle. In addition to these products one recovers from the neck of the retort also a small amount of arsenious oxide in the form of small crystals. The distillation residue is a carbonaceous material which gives off a garlic odor when heated over hot coals.
>
> The first liquid to distill reacts with caustic alkali with strong effervescence, generating at the same time a garlic odor so strong that it is impossible to breathe. Neither vinegar nor other compounds with very strong odors can destroy the odor that remains in vessels that have been impregnated with this liquid. It is dissipated only after several months of exposure to fresh air.
>
> The last liquid to distill, which is red-brown, deposits, after some time, a solid of a beautiful yellow color which I suppose to be a metallic substance that was entrained during the distillation and, due to its weight, precipitates to the bottom of the receiver.

Cadet says further:

> ... if these liquids are exposed to air they fume like phosphorus and generate a very strong odor of garlic. These vapors do not inflame when exposed to a burning candle but on opening the grease-sealed receiver containing the two liquids to the air they caused immediate inflammation of the grease, which surprised me very much.

Cadet very wisely did not pursue this matter further. After all, he really had no way of investigating the composition of his "liqueur fumante". Neither the experimental techniques to do so nor the conceptual basis for understanding the compounds contained in his fuming distillate were available at that time. In 1757 the phlogiston theory of combustion still prevailed. In 1757 Lavoisier was only a boy of 14 and his "revolution in chemistry", which toppled the phlogiston theory, beginning with his experiments on combustion, did not start until 1772.

Louis-Claude Cadet de Gassicourt[2] was one of thirteen children of Claude Cadet, a Parisian surgeon, who died when Louis-Claude was 14. The Cadet children were taken in by friends in various locations, Louis-Claude going to the village of Gassicourt. In later years he appended "Gassicourt" to his name. After he had completed his studies at the Collège des Quatre-Nations, he was apprenticed in pharmacy and chemistry and

---

[1] Cadet de Gassicourt, L. C. "Suite d'Expériences nouvelles sur l'Encre sympathique de M. Hellot qui peuvent servir à l'analyse du Cobolt; et Histoire d'une liqueur fumante, tirée de l'Arsènic" *Memoires de Mathématique et de Physique. Presentés à l'Académie Royale des Sciences par diverse Savans et lûs dans ses Assemblées.* Tome Troisième, MDCCLX (1760), p 623. These results were communicated to the Royal Academy of Sciences in 1757, reported on favorably by two academicians, Bourdelin and Lassone, in January 1758, and finally published in 1760.

[2] Biographical accounts (in English) of L.-C. Cadet de Gassicourt: (a) Berman, A. In *Dictionary of Scientific Biography*; Gillispie, C. C., Ed.; Charles Scribner's Sons: New York, 1970; Vol. III, pp 4−6. (b) Berman, A. *Bull. History Med.* **1996**, *40*, 101. (c) Partington, J. R. *A History of Chemistry*; Macmillan: London, 1962; Vol. III, p 96.

10.1021/om0101947 CCC: $20.00

later worked in the apothecary shop of the Geoffroys, father and son, both of whom were members of the Royal Academy of Sciences. Through their intervention, Cadet obtained a position for six years (1753−1759) at the Hotel Royal des Invalides in Paris. In addition to further training in pharmacy, he carried out research in chemistry, and it was here that he discovered his “fuming liquid”. His other, earlier work included an improved preparation of potassium acetate and the analysis of mineral waters. After the six-year period, he qualified as apothicaire-major, and he was active with the military in later years, reorganizing the pharmaceutical services of the French armies stationed in Germany in 1761. After he had completed this training period at the Hotel des Invalides, Cadet purchased an apothecary’s laboratory and shop on the rue St. Honoré in Paris.

However, Cadet continued his research in chemistry. He became a well-known pharmacist-chemist and was elected to the Royal Academy of Sciences in 1766. He actively collaborated with his fellow chemist-academicians. Lavoisier and Cadet were friends, and they collaborated in 1772, together with Macquer, on an investigation of the effect of heat on diamonds. In 1774 Cadet reported that calcining HgO results in formation of elemental mercury, a fact that was disputed by his fellow academician Baumé. This matter was investigated by a committee composed of Lavoisier, Brisson, and Sage, who reported to the Academy of Sciences that Cadet was right. Curiously, none of these chemists involved in this dispute realized that a gas (O_2) was given off in this process. It was Priestly and Scheele who independently discovered oxygen at about the same time. Cadet, it may be noted, did not espouse the “New Chemistry” being developed by Lavoisier, but did not oppose it, remaining noncommittal instead. He also collaborated with Berthollet and Lavoisier at the Paris Mint and was appointed Royal Commissioner at the Sèvres porcelain factory.

Cadet married Marie Thérèse Boisselet in 1771, who came accompanied by a 2-year-old son fathered by Louis XV. The boy was adopted by Cadet as Charles-Louis Cadet and had a distinguished career. After literary and political activities, he became a leader in French pharmaceutical circles and an enthusiastic supporter of the “New Chemistry” of Lavoisier.

Cadet’s intriguing chemistry was repeated by three brave French chemists in Dijon, Guyton de Morveau, Maret, and Durande, who reported in 1778[3]:

> The red liquid, even when it is cooled, retains the ability to fume every time the flask in which it is contained is opened and spreads the same horrible odor which nothing can destroy....
>
> We wanted to analyze the solid that the red liquid deposits in the bottom of the flask. To do this we began carefully to decant most of the upper liquid. The remaining portion we poured carefully onto a filter paper. After only a few drops, heavy, nauseating fumes became apparent, forming a column from the flask to the ceiling. The material on the filter paper began to boil slightly and then came a beautiful rose-colored flame which lasted a few moments.

Although they were exposed to this horrible and penetrating odor for some time, these authors said that they did not notice any lasting bad effects except for a very disagreeable irritation of the throat.

In 1804, another French chemist, Louis Jacques Thénard, reported on his investigation of Cadet’s fuming liquid. He claimed that the gases given off during the As_2O_3/CH_3CO_2K distillation contained “l’hydrogène arsènique” (AsH_3), carbon dioxide, and hydrocarbons, while As_2O_3 and metallic arsenic sublimed into the neck of the retort. The distillate contained two layers, the upper being an aqueous acetic acid solution of the liquid in the lower layer. It was the latter which was the origin of the horrible stench and the spontaneous inflammability in air. Oxidation of this liquid with chlorine was studied, and Thénard concluded that it was a “sorte d’acetite oleo-arsènical”, a complex arsenical acetate.

There matters stood until some 25 years later, until a brief study by J. B. Dumas, and immediately afterward, the thorough investigations of R. W. Bunsen, investigations, which in the words of Adolf von Baeyer, “showed how even the most difficult problems in chemical experimentation can be solved by the hands of a master”.

Part II. The Investigations of R. W. Bunsen

All of the early studies of Cadet’s fuming liquid were qualitative in nature, made difficult by the liquid’s horrible stench and inflammability, and it was not until the investigations of Robert Wilhelm Bunsen during 1837−1843, work begun at the Polytechnic School of Kassel and continued in 1839 at the University of Marburg, that more useful information concerning Cadet’s fuming liquid became available. The results of these studies were published in seven papers.[5−12] Bunsen was an outstanding experimentalist and a skilled glassblower who designed and made his own glassware, and this expertise was brought to bear with great success in these studies. Bunsen did not fool around with small-scale preparations, although he was aware of the repulsive and dangerous nature of the expected products.[7] Starting out with one kilogram of a 1:1 by weight As_2O_3/CH_3CO_2K mixture in a glass retort, he heated it very slowly to red heat in a sand bath. As Cadet had reported, two liquid layers and a solid phase collected in the receiver. The solid was a reduced arsenical material, the lower, heavier liquid layer was

---

(3) Guyton de Morveau, L. B.; Maret, H.; Durande, J. F. *Élemens de Chymie théoretique et pratique*; Dijon, 1778, Vol. III, p 39.

(4) Thénard, L. J. *Ann. Chim.* **1804**, *52*, 54. (Thénard (1777−1857), professor at the Collège de France, among other things, studied the reduction of alkali metal oxides with iron, the alkali metal amides, obtained elemental boron by reduction of boric oxide, discovered hydrogen peroxide.)

(5) Bunsen, R. W. *Poggendorf's Ann.* **1837**, *40*, 219.

(6) Bunsen, R. W. *Poggendorf's Ann.* **1837**, *42*, 145.

(7) Bunsen, R. W. *Ann.* **1837**, *24*, 271.

(8) Bunsen, R. W. *Ann.* **1839, *3*1**, 175.

(9) Bunsen, R. W. *Ann.* **1841**, *37*, 1.

(10) Bunsen, R. W. *Ann* **1842**, *42*, 14.

(11) Bunsen, R. W. *Ann.* **1843**, *46*, 1.

(12) Bunsen’s cacodyl papers were collected and published in Volume 27 of *Ostwald’s Klassiker der exakten Wissenschaften* (Wilhelm Engelmann: Leipzig, 1891; edited by Adolf von Baeyer) under the title *Untersuchungen über die Kakodylreihe*. This little book is useful in that Baeyer’s explanatory comments at the end help the reader to understand the background (e.g., Berzelius’ radical theory), and it also translates Bunsen’s chemical formulas, which were based on Berzelius’ 1826 atomic weight scale, into recognizable formulas based on the atomic weights current in 1891 (and still much the same today).

a brown oil, and the top layer was found to be a mixture of water, acetone, and acetic acid, containing also some of the arsenic product of the lower layer and some arsenious acid. Gas evolution occurred during the distillation—mostly carbon dioxide, methane, and ethylene, but (contrary to Thénard) no arsine (which explains why the earlier French investigators lived to tell the tale). However, Bunsen warns that the gases, presumably containing entrained organoarsenicals, are extremely irritating to the respiratory system. He stresses that this preparation should be carried out in the open air because of these noxious gases. Such a kilogram-scale preparation typically gave ~150 g of the red-brown liquid. Purification of the latter required several water washing, distillation, and drying operations, all carried out with exclusion of air, under a CO_2 atmosphere. The final "pure" product, to which Bunsen gave the name "Alkarsin" (derived from *Alk*ohol + *Arsin*, since he regarded it as a compound that had arsenic in place of the OH function of an alcohol), and reported its properties in detail:[7] it is a clear, colorless liquid, heavier than and not miscible with water. Its odor is extremely repulsive, reminiscent of the odor of arsine. Even small amounts are extremely lachrymatory and cause an almost unendurable, long-lasting irritation of the nasal mucous membranes. Exposure to the vapors for a longer time causes nausea and oppression of the chest. The liquid causes violent itching when in contact with the skin. Its taste [!!] is similar to its odor and it is very toxic. On exposure to air or oxygen, thick white fumes are evolved in an exothermic reaction, resulting in a pale flame with formation of water, CO_2 and As_2O_3, the latter as a white smoke. All in all, the first organometalloidal compound was quite a nasty customer!

Since it inflamed in air, the "Alkarsin", like elemental phosphorus, was best stored under water (no inert atmosphere boxes or Schlenk apparatus then), but slow air oxidation while it is stored in this way causes decomposition to water-soluble products. Such slow, controlled air oxidation of Alkarsin, Bunsen found, gave two products: arsenious acid and a crystalline compound that he named Alkargen, which contained carbon, hydrogen, oxygen, and arsenic. The latter compound, in contrast to the toxic Alkarsin, appeared not to be toxic. Bunsen reports[7] that frogs were unaffected by a dose of 1 grain (0.0648 g) of Alkargen, while they died quickly when given only 1/10 grain of As_2O_3.

The constitution of Bunsen's Alkarsin was, of course, of interest. Bunsen carried out C,H analyses (22.46% C, 5.75% H), but the %As was calculated by difference (71.8%) because the usual chemical degradation procedures to release the arsenic were initially unsuccessful. This gave an empirical formula of C_2H_6As. Vapor density measurements established a dimeric formula, $C_4H_{12}As_2$.

A few years before Bunsen started investigating Cadet's fuming liquid, a French chemist, Jean Baptiste Dumas, had become interested in this material.[13] Attempts to prepare a phosphorus analogue of Cadet's liquid were unsuccessful, so, reluctantly, as he said (because of the toxicity and so very unpleasant smell), he prepared Cadet's liquid and analyzed it (as early as 1828 and 1832, he said). His C and H percentages were essentially the same as those obtained by Bunsen. The arsenic analysis gave trouble. In a number of experiments in which the oxidation of the heavy layer of the distillate (i.e., the Alkarsin) with aqua regia was attempted, only one proceeded without explosion. That gave an arsenic content of 69.3%, which later was disputed by Bunsen. The C,H results are close to those calculated for the empirical formula of C_2H_6As. Apparently, Dumas did no further work on Cadet's fuming liquid and did not report his results until Bunsen had published his first papers.

Berzelius, the great Swedish inorganic chemist, was interested in Bunsen's work, and Bunsen kept him informed of his results. Berzelius reported and commented on this work in his annual *Jahresbericht* volumes. Thus in 1839 he wrote:[14] "An extremely important discovery has been made by Bunsen, in the investigation of the well-known fuming, self-inflammable liquid obtained when anhydrous acetate of potash is distilled with arsenious acid. From this body, Bunsen has prepared several substances whose properties resemble those of an organic compound, in which, however, arsenic enters as an elementary constituent."

Berzelius suggested to Bunsen that his Alkarsin must contain oxygen (since both starting materials contained oxygen). Another analysis by Bunsen of another sample of Alkarsin did indeed show this to be the case.[8] The analysis (average of two: C, 21.66%; H, 5.30; As, 65.75; O, 7.24) corresponds to an empirical formula of $C_4H_{12}As_2O$.[15]

Berzelius championed a "radical" theory"[17] and thought that Bunsen's Alkarsin fit in very nicely. In his 1841 *Jahresbericht*[16] he wrote: "In the last German edition of my handbook, I gave what I considered the probable theoretical views regarding this substance (i.e., the oxygen-containing Alkarsin), namely that it contains the compound radical $C_4H_{12}As_2$, similar to the radicals contained in organic bodies, for which I have suggested to Bunsen the name *kakodyl* (Greek, stinking) in consequence of the nauseous smell of its compounds."

Bunsen discontinued calling his product Alkarsin and henceforth used the kakodyl (cacodyl in the English literature) nomenclature and used the abbreviation *Kd* for the cacodyl "radical", $C_4H_{12}As_2$. His "Alkarsin" thus became "cacodyl oxide".

---

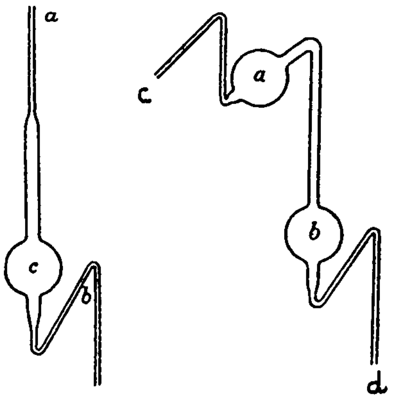
(13) Dumas, J. B. *Ann.* **1838**, *27*, 148. (Dumas (1800–1884), professor at the Sorbonne, devised methods for the determination of nitrogen in organic compounds and a method for the determination of vapor densities. His studies of Cl-for-H substitution in organic molecules were of great importance in the development of the "type theory" of organic structure.)

(14) Berzelius, J. J. *Jahresber.* **1839**, *18*, 487. (The English translations of these excerpts from the *Jahresberichte* are quoted from H. Roscoe's Bunsen Memorial Lecture, ref 21b.)

(15) Variability of analytical results is not surprising, as later workers showed that Bunsen's Alkarsin is not a single compound, containing instead $(CH_3)_2AsOAs(CH_3)_2$ and $(CH_3)_2As-As(CH_3)_2$ as the major components. This is understandable in view of the difference in the boiling points of the two compounds: $(CH_3)_2AsOAs(CH_3)_2$ bp 170 °C; $(CH_3)_2As-As(CH_3)_2$ bp 120 °C. The composition of the distillate thus depends on how carefully the fractional distillation was performed.

(16) Berzelius, J. J. *Jahresber.* **1841**, *20*, 526.

(17) The "radicals" of Bunsen's time are not the same as the "radicals" of today, the electron and the electron pair concept being unknown. Here the "radical" is equivalent to a stable group of atoms that retains its identity in its reactions and in its formation of compounds with other (generally electronegative) atoms or groups. Chemists of that day hoped to be able to isolate such "radicals", and Berzelius and Bunsen thought that in cacodyl they had such a stable radical since it formed compounds with electronegative groups.



(a) (b)

Figure 1. "Bunsen-ware" used in his cacodyl chemistry (from ref 10).

Bunsen did not try to establish the actual composition of his Alkarsin in his subsequent research, but he developed its chemistry quite extensively, preparing a number of pure derivatives containing the cacodyl [$(CH_3)_2As$ in modern terms] group: the fluoride, chloride, bromide, iodide, cyanide, sulfide, and selenide, to name a few.[9-11]

It is of interest to consider the details of Bunsen's preparation of what he thought was and called the "cacodyl radical", actually the cacodyl dimer, tetramethyldiarsine, $(CH_3)_2As-As(CH_3)_2$,[18] by the action of zinc on cacodyl chloride, $(CH_3)_2AsCl$, the latter having been prepared by the reaction of highly concentrated HCl with "cacodyl oxide" (i.e., Alkarsin) as its $HgCl_2$ adduct, followed by distillation of the reaction mixture.[19] Bunsen wrote the equation

$$\left.\begin{array}{c} \mathrm{KdO} + \mathrm{Hg_2Cl_4} \\ \mathrm{H_2Cl_2} \end{array}\right\} \begin{array}{l} \mathrm{KdCl_2} \\ \mathrm{H_2O} \\ \mathrm{Hg_2Cl_4} \end{array}$$

which, translated into today's chemistry and using today's atomic weights, would be

$$[(CH_3)_2As]_2O\cdot 2HgCl_2 + 2HCl \rightarrow 2(CH_3)_2AsCl + H_2O + 2HgCl_2$$

In the gas phase (bp a bit over 100 °C), cacodyl chloride is pyrophoric in air; the liquid, when heated in air, burns with a pale arsenic flame. Its odor is much worse than that of Alkarsin, as are its physiological effects.

The cacodyl chloride thus prepared required no further purification but had to be dried in the absence of air. This was accomplished by means of the glass apparatus that Bunsen made for this purpose (Figure 1a). The bulb *c* was charged with drying agents (anhydrous $CaCl_2$ and CaO), and the air was completely displaced from the apparatus by blowing dry, gaseous CO_2 through the open end *a*. The apparatus was stored with both ends sealed. For use, end *a* was opened and attached to a hand pump by means of a short piece of rubber tubing. Then end *b* was opened and immersed into the cacodyl chloride through the aqueous HCl layer under which it was stored. The chloride was drawn into bulb *c*, and both ends were sealed off. After several days the cacodyl chloride was dry and ready for use. Its conversion to the cacodyl dimer was effected in the glass apparatus shown in Figure 1b. Zinc metal in the form of carefully cleaned (with dilute H_2SO_4 and H_2O) and dried small shavings of foil was charged into bulb *a* prior to completion of the apparatus (no ground glass or Teflon joints then). All air was displaced with dry CO_2, and the cacodyl chloride was drawn into bulb *a* via *c*. The ends were sealed, and the Zn/cacodyl chloride mixture was heated at ~100 °C in a water bath. The zinc readily dissolved without gas evolution. Heating was continued until bulb *a* on cooling contained a solid mass of zinc chloride. The apparatus was warmed, and then end *d* was opened under cold, boiled (deaerated) water. The gas in the apparatus was expelled by heating, and in its place water was sucked in. The apparatus was resealed and tilted to bring the water into bulb *a*. In a short time the zinc chloride dissolved, leaving the excess of zinc and impure cacodyl dimer as an oily liquid. The latter was dried in the drying apparatus (Figure 1a) and returned to the reaction apparatus (Figure 1b) and subjected to another reaction with zinc to ensure complete consumption of the chloride. The product now was a clear liquid that crystallized in large part at −6 °C. The remaining liquid portion was reacted again with zinc. This treatment was repeated two more times. Finally, the cacodyl dimer was distilled (under CO_2), after drying, from bulb *a* of the reaction apparatus into bulb *b*.

This procedure is described in such detail to show the laborious, tedious, and painstaking effort that was required to work with the cacodyl compounds. The cacodyl dimer is as spontaneously inflammable in air as white phosphorus, and utmost care was required in its preparation and handling to avoid all exposure to air in order to obtain a pure, oxygen-free sample. All of Bunsen's preparative experiments were carried out with such care, and equal attention to detail was apparent in his analytical work, the detailed description of which occupied a large fraction of each of his papers.

Accidents with cacodyl compounds could have serious consequences. During his study of cacodyl cyanide, $(CH_3)_2AsCN$, prepared by reaction of "cacodyl oxide" with a concentrated aqueous solution of mercuric cyanide, an explosion cost Bunsen the partial sight of his right eye and, as Roscoe reports, "Bunsen was nearly poisoned, lying for days between life and death." Bunsen recovered and completed his study of cacodyl cyanide, a most unpleasant compound. After distillation of the "cacodyl oxide"/$Hg(CN)_2$ reaction mixture, the cacodyl cyanide formed beautiful, prismatic crystals underneath the water layer. These were quite volatile (mp 32.5 °C). They were dried by pressing them between sheets of blotting paper. Bunsen notes that it is absolutely necessary to carry out this operation in the open air while breathing through a long glass tube that extends to fresh air far beyond the volatile crystals. And well

---

[18] Rather than referring to $Me_2As-AsMe_2$ as the "cacodyl radical" (as did Bunsen), I shall refer to it as the "cacodyl dimer", reserving the name "cacodyl" for the Me_2As group.

[19] A simpler preparation of $(CH_3)_2AsCl$ by the reaction of pure cacodyl oxide with hydrochloric acid was reported later: Baeyer, A. *Ann.* **1858**, *107*, 257. (Baeyer (1835−1917) pupil of Bunsen and Liebig; one of the great German organic chemists. Determined constitution of indigo, first synthesis. Studied phthaleins, uric acid, purines, terpenes. Nobel Prize in 1905.)

might this compound be avoided! Bunsen reports that the vapor from 1 grain (0.0648 g) of cacodyl cyanide in a room produces sudden numbness of the hands and feet, and dizziness and insensibility to the point of unconsciousness. The tongue becomes covered with a black coating. These effects, however, are only temporary, with no lasting problems. (Bunsen, it may be noted, lived to the ripe old age of 88.)

Mention also should be made of cacodylic acid (originally Alkargen), which Bunsen wrote as KdO_3 and which in its modern formula is $(CH_3)_2As(O)OH$. This compound is best prepared by oxidation of cacodyl oxide with HgO. This reaction is very exothermic; when carried out in aqueous medium, the water begins to boil and elemental mercury precipitates. The equation Bunsen writes is

$$\left.\begin{matrix} KdO \\ 2HgO \\ H_2O \end{matrix}\right\} \begin{matrix} H_2O + KdO_3 \\ Hg_2 \end{matrix}$$

An almost theoretical yield of cacodylic acid was obtained, which was purified by recrystallization from alcohol. Cacodylic acid is remarkably stable toward strong oxidizing agents: fuming nitric acid and concentrated $H_2SO_4/K_2Cr_2O_7$ are without effect. Although it is water-soluble and contains 71.5% As, cacodylic acid, surprisingly, was found not to be toxic to rabbits when 6 grains were injected into the stomach, or 7 grains into the jugular vein. Remarkable also is that cacodylic acid is odorless. Its thermal stability is high: no decomposition occurred up to 200 °C, at which temperature it melted. It thus is an atypical cacodyl compound, but then, the arsenic atom in cacodylic acid is in oxidation state V, not III, as in the other cacodyl compounds.

There is not space to discuss the other known cacodyl compounds, and the reader is directed to ref 20 for an excellent and thorough coverage of the extensive series of cacodyl compounds that Bunsen prepared. Looking back at this body of work today, some 160 years later, we cannot help but admire Bunsen's experimental skills, ingenuity, and persistence. This research on highly air-sensitive, highly toxic, and terribly odiferous compounds was carried out without the benefit of the inert atmosphere boxes, Schlenk lines, efficient hoods, and ground glassware that we are used to today. The laboratories of those days had poor ventilation. In 1852 Bunsen moved to the University of Heidelberg— the reader may be interested in the laboratories that he found there—as reported by an English co-worker of his, Henry Roscoe:[21b]

> When he first came to Heidelberg in the summer of 1852, Bunsen found himself installed in Gmelin's old laboratory. This was situated in the buildings of an ancient monastery, and there we all worked. It was roomy enough; the old refectory was the main laboratory, the chapel was divided into two, one half became the lecture-room and the other a storehouse and museum. Soon the number of students increased and further extensions were needed, so the cloisters were enclosed by windows and working benches placed below them. Beneath the stone floor at our feet slept the dead monks, and on their tombstones we threw our waste precipitates! There was no gas in Heidelberg in those days; nor any town's water supply. We worked with Berzelius's spirit lamps, made our combustions with charcoal, boiled down our wash-waters from our silicate analyses in large glass globes over charcoal fires, and went for water to the pump in the yard. Nevertheless, with all these so-called drawbacks, we were able to work easily and accurately. To work with Bunsen was a real pleasure. Entirely devoted to his students, as they were to him, he spent all day in the laboratory, showing them with his own hands how best to carry out the various operations in which they were engaged.

Bunsen obtained a new laboratory in 1855.

Figure 2. Robert Wilhelm Bunsen (reproduced courtesy of the Library and Information Centre of The Royal Society of Chemistry).

We cannot go on to the further development of the chemistry of our cover molecule without telling something about Bunsen, the man who contributed so much to its story, since he was one of the great chemists of the nineteenth century.[21]

Bunsen (Figure 2) was born in 1811. His father was

---

(20) Morgan, G. T. *Organic Compounds of Arsenic and Antimony*; Longmans, Green, and Co.: London, 1918; Chapter 1, pp 1−19.

(21) Biographical accounts of R. W. Bunsen: (a) Schacher, S. G. In *Dictionary of Scientific Biography*; Gillispie, C. C., Ed.; Charles Scribner's Sons: New York, 1976; Vol. II, pp 586−590. (b) Roscoe, H. *J. Chem. Soc.* **1900**, *77*, Part 1, 513−554. (c) Partington, J. R. *A History of Chemistry*; Macmillan: London, 1964; Vol. 4, pp 281−293. (d) Fuchs, O. In *Das Buch der grossen Chemiker*; Bugge, G., Ed.; Verlag Chemie: Weinheim, 1929; 1965; Vol. 2, pp 78−91. (e) Oesper, R. E. *J. Chem. Educ.* **1927**, *4*, 431. (An account of R. W. Bunsen, the person.)

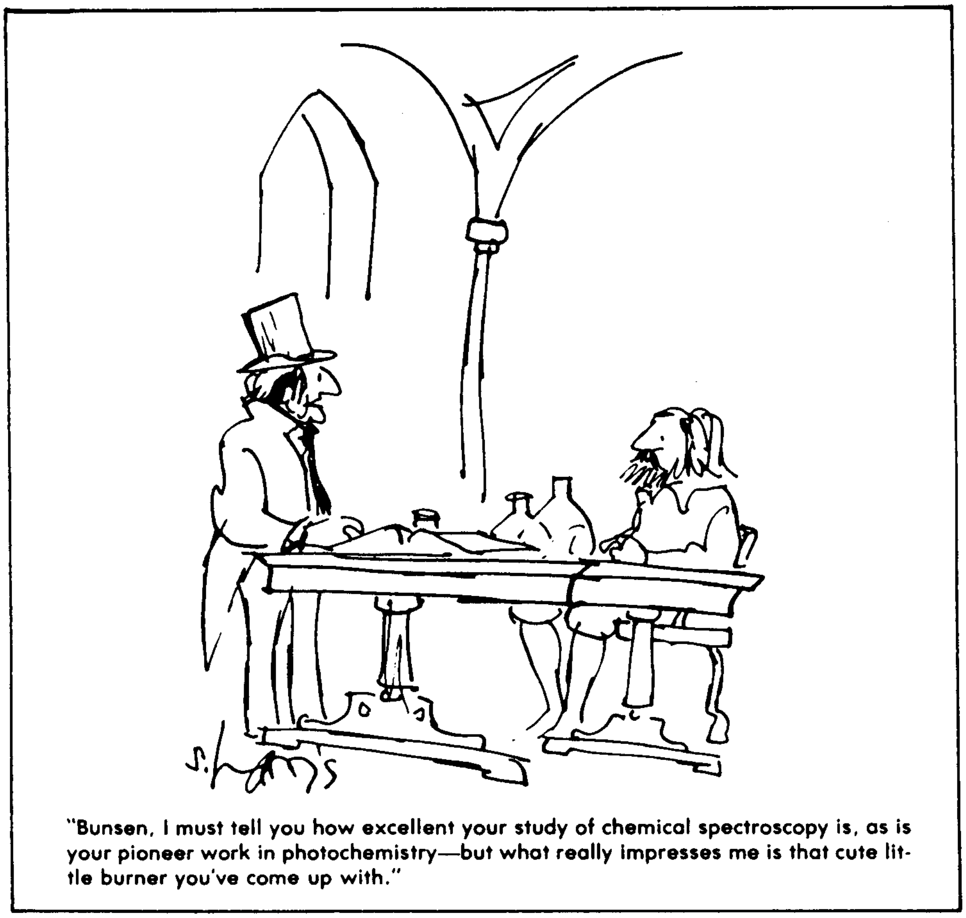


Figure 3. Copyright 1979 by Sidney Harris, *Current Contents* (reproduced with permission).

Christian Bunsen, Chief University Librarian and professor of modern philology at the University of Göttingen. He entered the University of Göttingen in 1828, at the age of 17, where he studied chemistry (under Friedrich Strohmeyer, the discoverer of cadmium), physics, minerology, and mathematics. He received his doctorate in 1831 (!), writing a thesis on the different types of hygrometers ("Enumeratio ac descriptio hygrometrorum"). Then followed a period of scientific travel throughout Europe, supported by a fellowship from the state of Hannover, during which he spent the winter of 1832−33 in Paris. There he worked in the laboratory of Gay-Lussac and attended lectures at the École Polytèchnique. He also visited Berlin, Vienna, Giessen (where he met Liebig), and Bonn. In the fall of 1834, he became Privatdozent at the University of Göttingen, where he began independent research. An appointment in chemistry at the Polytechnic School of Kassel as Friedrich Wöhler's successor followed in 1836. Bunsen was appointed extraordinary professor of chemistry at the University of Marburg in October 1839; promotion to full professor came in 1842. A call from the University of Breslau was accepted in 1851, but Bunsen's stay there was only a short one. In 1852 he accepted an appointment at the University of Heidelberg to the chair in chemistry as successor to Leopold Gmelin, a position that he retained until his retirement in 1889 at the age of 78.

After the six years devoted to the study of the cacodyl compounds, Bunsen, perhaps understandably, never returned to organic chemistry. His research for the rest of his career covered broad areas of analytical and physical chemistry. In connection with an investigation of the industrial production of cast iron in Germany and England, he of necessity developed new methods for the handling and analysis of gases, which found wide application by others. His research during the 1840s and 1850s resulted in a number of improvements in the galvanic battery, including invention of the "Bunsen (carbon−zinc) battery". Using electrochemical techniques, he isolated various metals, generally from their molten chlorides: Cr, Mg, Na, Al, Li, Ca, Sr, Ba, La, Ce. The commercial manufacture of magnesium was undertaken, and the specific heats of some of these metals were measured. To do this, Bunsen devised a new ice calorimeter.

Upon the advent of coal gas in Heidelberg, Bunsen began his experiments on a laboratory gas burner. The result was the well-known "Bunsen burner", which is still in use today. As Roscoe says:[21b] "The invention which perhaps more than any other has popularised the name of Bunsen is that of his celebrated burner." (Figure 3) Using his burner, Bunsen developed flame color tests for elements that still are useful in qualitative inorganic analysis.

With Roscoe, Bunsen studied the photochemically initiated gas-phase $H_2 + Cl_2$ reaction in great detail and, more generally, the chemical action of light. However, it is the investigations of Bunsen and Kirchhoff, professor of physics at Heidelberg whom Bunsen had first met in Breslau, and whose appointment at Heidelberg he had facilitated, on the chemical applications of spectroscopy which, perhaps, were the most important and of lasting impact. They recognized that analysis of the emission spectra of celestial bodies and terrestrial matter could serve in determination of their elemental composition. A consequence of this was their discovery of Cs and Rb, both hitherto unknown elements.

These are just some highlights of Bunsen's long and distinguished career in research, good summaries of which are given in refs 21b–d. Bunsen also was a dedicated teacher, giving his lectures on general chemistry (with lecture demonstrations) every morning of the week from 8:00 to 9:00 in the summer term and from 9:00 to 10:00 in the winter term. His lectures dealt with the facts, not the theories, of chemistry. This was true also in his research: he did not take part in the discussions of the chemical theories of the day which were raging in Europe in his time. He was an experimental chemist and a superb one at that. His contributions to physical chemistry, in particular, were exceptionally important, and in recognition of these, the German physical chemists call their professional society the "Deutsche Bunsen-Gesellschaft für Physikalische Chemie".

Part III. Later Work on Cadet's Fuming Liquid and the Cacodyl Compounds

In his 1842 *Jahresbericht*,[22] Berzelius wrote about Bunsen's cacodyl results: "By this investigation Bunsen has made his name memorable. Chemical science is bound to acknowledge its debt to him for the investigation of a subject at once so important and so dangerous—an investigation of which it may well be said that it leaves little to be desired." And in 1845:[23] "Bunsen has now concluded his investigation on kakodyl. ... The research is a foundation stone of the theory of compound radicals of which kakodyl is the only one, the properties of which in every particular correspond with those of the simple radicals." Of course, Berzelius was pleased since it appeared that Bunsen had obtained strong experimental support for his compound radical theory. However, there remained some unanswered questions about Cadet's fuming liquid. In particular, there was the question of the composition of the red-brown distillate, after purification. Analyses in agreement with empirical compositions of $C_4H_{12}As_2$ and $C_4H_{12}As_2O$ had been obtained. Bunsen opted for the latter and called it "cacodyl oxide", the oxygen derivative of the cacodyl "radical", $C_4H_{12}As_2$. However, there was a problem: the controlled, slow air oxidation of purified Cadet's liquid, followed by dissolution of the product (a crystal-containing syrup) in water and distillation of the aqueous solution, gave a liquid whose analysis gave the same empirical formula, $C_4H_{12}As_2O$, as "cacodyl oxide". This compound was an oily liquid with a characteristically penetrating odor with the same solubility properties as Bunsen's "cacodyl oxide". However, it differed from the latter in that at room temperature it did not fume and ignite in air. However, in air at 50–70 °C, its vapors exploded violently. Bunsen thought that it was an isomer of some kind and called it "paracacodyl oxide". However, he also considered the possibility that it was pure cacodyl oxide, while the Alkarsin ("cacodyl oxide" as he called it), thought to be bona fide cacodyl oxide, was impure, containing some "cacodyl radical" which caused its inflammability. Bunsen finally rejected the latter possibility because "cacodyl oxide" and "paracacodyl oxide" reacted differently with $Hg(CN)_2$. This question was resolved by Adolf Baeyer,[19] who prepared pure cacodyl oxide by the reaction of aqueous KOH with cacodyl chloride. Distillation of the aqueous reaction mixture, followed by drying of the oil which was obtained and fractional distillation under CO_2, gave highly pure oxide as a mobile liquid that did not fume in air and had an unbearable odor and that was identical in all respects with Bunsen's "paracacodyl oxide". Baeyer found that it is the so-called "cacodyl radical" ($Me_2As-AsMe_2$) that reduces $Hg(CN)_2$ to give $(CH_3)_2$ AsCN and elemental mercury. The oxide, on the other hand, does not reduce $Hg(CN)_2$.

Thus Bunsen's Alkarsin, which he later called "cacodyl oxide", in reality is a mixture of $(CH_3)_2AsOAs(CH_3)_2$ and $(CH_3)_2As-As(CH_3)_2$. It is the latter that is pictured on our cover because it is the more important one of the two. The relative proportions of these compounds in the purified distillate no doubt depends on how the distillation of the As_2O_3/CH_3CO_2K mixture is carried out and how the further purification of the distillate is performed.

There also was the question as to what exactly was the "cacodyl radical". Hermann Kolbe, a strong supporter of the "radical" theory on the basis of his studies of the electrolysis of carboxylic acid salts (which he believed produced "radicals"—and which actually does involve real free radicals) proposed that cacodyl is a combination (a "conjugate compound" as he called it) of two methyl radicals and an As atom,[24] i.e., $(C_2H_3)_2As$, as he wrote it (old atomic weights), $(CH_3)_2As$, as we write it today. In his "Dictionary of Chemistry", in 1849, he listed all known cacodyl compounds as dimethylarsino compounds.[25] Edward Frankland, also a supporter of the radical theory, was in Bunsen's laboratory in Marburg when he discovered the ethyl- and methylzinc compounds.[26a,b] Frankland had spent three months in 1847 in Bunsen's laboratory in Marburg working with Hermann Kolbe, in search of organic "radicals", studying the action of potassium on nitriles. On his return to England, Frankland, while at Queenwood College, investigated the reaction of ethyl iodide with potassium

---

[22] Berzelius, J. J. *Jahresber.* **1842**, *21*, 503.

[23] Berzelius, J. J. *Jahresber.* **1845**, *24*, 640.

[24] (a) Kolbe, H. *Ann.* **1850**, *75*, 211. (b) Kolbe, H. *Ann.* **1850**, *76*, 1. (c) Kolbe, H. *J. Prakt. Chem.* **1881**, *23*, 316. (Kolbe (1818–1884), champion of the radical theory, discovered many new organic compounds, resisted new ideas of stereochemistry, and fought them vigorously until his death.)

[25] Kolbe, H. *Handwörterbuch Chem.* **1849**, *4*, 218–245.

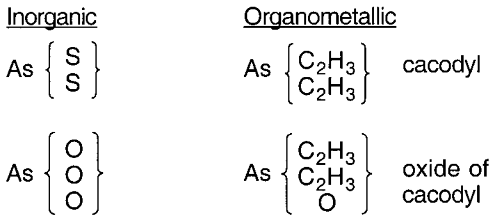
[26] (a) Frankland, E. *J. Chem. Soc.* **1849**, *2*, 297. (b) Frankland, E. *Ann.* **1849**, *71*, 213. (c) Frankland, E. *Philos. Trans.* **1852**, *142*, 417 (pp 438–444).

[27] (a) Cahours, A.; Riche, A. *C. R. Acad. Sci.* **1853**, *36*, 1001. (b) Cahours, A.; Riche, A. *C. R. Acad. Sci.* **1854**, *39*, 541; *Ann.* **1854**, *92*, 361. (Cahours (1813–1891), professor at École Polytechnique, organic chemist, prepared diverse new organic compounds; prepared Et_4Sn and propyl- and butyltin compounds.)

as a route to the ethyl "radical". That reaction, being a bit too violent, caused him to switch metals, using zinc instead of potassium. The sealed tube containing the resulting reaction mixture he took with him to Marburg on his next, longer, visit to Bunsen's laboratory in 1849, and there he continued his study of RI + Zn reactions in the hope of obtaining isolable organic "radicals". The analogy that guided him must have been Bunsen's reaction of cacodyl chloride + Zn → "cacodyl radical", so RI + Zn → R "radical". In any case, the isolated products were the R_2Zn and RZnI compounds, and so the first main group organometallic compounds were in hand. In 1849 Frankland also reported, without providing details, that reaction of ethyl iodide with elemental arsenic gave a product that had "a most insupportable odor" that greatly resembled that of the "cacodyl radical".[26b] He suggested that use of methyl iodide in place of ethyl iodide "would probably yield cacodyl". Frankland acknowledged the importance of Bunsen's cacodyl work some years later:

> The beneficial influence which the discovery of cacodyl has exerted upon the development of sound views in organic chemistry, and the pursuit of rational paths of research, can scarcely be over-estimated, since the support which it gave to the theory of compound organic radicals, enabled that theory to exist and to bring forth abundant fruits, throughout a period in the history of science when there was but feeble evidence of its truth, and until those researches, both of supporters and antagonists, finally established the fundamental accuracy of that theory.

Frankland in his early (1849) work considered his organometallic products to be compound radicals and compared them to the cacodyl radical, which he, like Kolbe, wrote as $(C_2H_3)_2As$.[26a,b] However, in 1852, Frankland, as he prepared organic compounds of other metals (Sn, Hg, As) and as others were preparing organic derivatives of still other metals, was on the way to his valence theory and looked at things a bit differently, making comparisons between the cacodyl compounds and inorganic arsenicals,[26c]



(based on the old atomic weight scale)

and proposing a system of nomenclature that nobody followed: $(C_2H_3)_2As$, bimethide of arsenic; $(C_2H_3)_2AsO$, bimethoxide of arsenic; $(C_2H_3)_2AsO_3$, bimetharsenic acid.

Returning to Cadet's fuming liquid, Cahours and Riche[27a] in 1853 reported carrying out the reaction of methyl iodide with elemental arsenic, a reaction Frankland had alluded to in 1849.[26b] A product was obtained that they did not identify and that had an unbearable odor of garlic and enflamed when warmed in air. It could have been $(CH_3)_2AsI$ or the cacodyl dimer (or a mixture of the two), the latter formed by reduction of the iodide by elemental arsenic. Also investigated was the reaction of methyl iodide with a sodium−arsenic alloy.[27b] The major products were $(CH_3)_3As$ and $[(CH_3)_4As]I$, but a low yield of cacodyl dimer also was obtained. The latter, they found, reacted violently with methyl iodide to give cacodyl iodide and tetramethylarsonium iodide, a reaction they wrote as

$$2\,(C^2H^3I) + 2\,(C^4H^6As) = (C^2H^3)^4As,\ I + C^4H^6AsI$$

Attempts to improve the yields of cacodyl dimer and cacodyl oxide in Cadet's fuming liquid have been reported. Baeyer was unsuccessful in this endeavor.[19] In 1906 Dehn and Wilcox were able to obtain cacodyl dimer, cacodyl oxide, and cacodylic acid in a combined yield of over 30% by more careful workup.[28] The gases evolved during the distillation were passed through a wash bottle containing HgO, which served to oxidize any uncondensed cacodyl oxide to cacodylic acid. The upper distillate layer also was treated with HgO, so all organoarsenic products were recovered. Dehn and Wilcox reduced all three cacodyl compounds with amalgamated Zn dust and hydrochloric acid to Me_2AsH, whose chemistry they studied in some detail. In the same year, a new and useful route to the cacodyl dimer, the reduction of cacodylic acid (which at that time was commercially available) by an excess of sodium hypophosphite in hydrochloric acid solution, was reported by Auger.[29] (A stoichiometric amount of sodium hypophosphite resulted in formation of cacodyl chloride.)

Seventy years after its discovery, the question of the composition of Cadet's fuming liquid was addressed by Valeur and Gailliot by means of its fractional distillation under an atmosphere of CO_2.[30,31] A low boiling (bp 50−52 °C) fraction was identified as trimethylarsine, and a fraction of boiling range 150−165 °C as a mixture of cacodyl dimer and cacodyl oxide. A large amount of distillation residue remained. The latter, when heated under reduced pressure, gave a blue liquid of bp 115−120 °C at 5 mmHg which did not crystallize at −80 °C but became extremely viscous. It was not spontaneously inflammable in air and had a very strong garlic odor. Its molecular weight, by cryoscopy in CO_2-saturated benzene, was 300. Brief exposure of the blue liquid to air discharged the color: It was proposed (but no

---

(28) Dehn, W. H.; Wilcox, B. B. *Am. Chem. J.* **1906**, *35*, 1; summary in *J. Am. Chem. Soc.* **1906**, *28*, 154.

(29) Auger, V. *C. R. Acad. Sci.* **1906**, *142*, 1151.

(30) Valeur, A.; Gailliot, P. *C. R. Acad. Sci.* **1927**, *185*, 779.

(31) Valeur, A.; Gailliot, P. *C. R. Acad. Sci.* **1927**, *185*, 956.

(32) Knoll, F.; Marsmann, H. C.; Van Wazer, J. R. *J. Am. Chem. Soc.* **1969**, *91*, 4986.

(33) Burns, J. H.; Waser, J. *J. Am. Chem. Soc.* **1957**, *79*, 859.

(34) Daly, J. J.; Sanz, F. *Helv. Chim. Acta* **1970**, *53*, 1879.

(35) Mundt, O.; Riffel, H.; Becker, G.; Simon, A. *Z. Naturforsch.* **1988**, *43b*, 952.

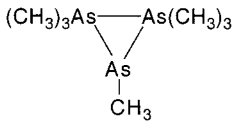
(36) Krause, E.; von Grosse, A. *Die Chemie der metall-organischen Verbindungen*; Gebrüder Bornträger: Berlin, 1937; pp 584−585.

(37) Lefebure, V. *The Riddle of the Rhine. Chemical Strategy in Peace and War*; The Chemical Foundation: New York, 1923.

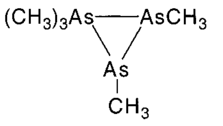
Table 1. Components of Cadet's Fuming Liquid (Ref 31)

compound	% in Cadet's liquid	boiling point	melting point	density
$(CH_3)_3As$	2.6	50 °C/760 mmHg	liquid at −80 °C	1.144
$(CH_3)_2AsOAs(CH_3)_2$	40	150 °C/760 mmHg	−57 °C	1.486
$(CH_3)_2As{-}As(CH_3)_2$	55.9	163 °C/760 mmHg	−5 °C	1.447
compounds **1** and **2** (mixture)	1.3	115−120 °C/5 mmHg	very viscous at −80 °C	1.647
$(CH_3As)_5$	0.2	190 °C/5 mmHg	+10 °C	2.150

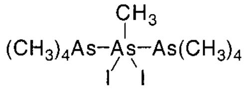
supporting evidence was provided) that the blue liquid was an inseparable mixture of two compounds, $(CH_3)_7As_3$ and $(CH_3)_5As_3$, for which structures **1** and **2** were written. These compounds made up only 1−2% of Cadet's liquid. Reaction of the **1**/**2** mixture with methyl iodide gave two crystalline, apparently separable methiodides, for which "structures" **3** and **4** were written. However, no characterization of these products was reported. Similar products were obtained on reaction of the **1**/**2** mixture with ethyl iodide.



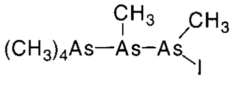
1



2



3



4

Valeur and Gailliot reported that filtration of Cadet's fuming liquid gave a brick-red solid, which they said was polymeric arsenomethane, $(CH_3As)_n$. Independent preparation of such a material was effected by reduction of methylarsonic acid, $CH_3As(O)(OH)_2$, with hypophosphorous acid. A liquid, bp 190 °C/5 mmHg, said to be cyclo-$(CH_3As)_5$, was obtained. This liquid polymerized spontaneously to give a brick-red solid similar to that obtained from Cadet's fuming liquid. When heated in a sealed tube for several hours, $(CH_3As)_5$ decomposed to a mixture of elemental arsenic, cacodyl dimer, and trimethylarsine. It was suggested that the arsenomethane was the precursor of the trimethylarsine and cacodyl dimer in Cadet's fuming liquid and that reactions of arsenomethane with trimethlarsine gave **1** and **2**. The Vaileur/Gailliot paper closes with a listing (Table 1) in which percentage yields of the components of Cadet's fuming liquid, as well as boiling and melting points and densities, are given. Unfortunately, no useful experimental details are provided, so this report is impossible to evaluate. What is needed is a repetition of such an investigation using modern procedures and instrumentation, in particular, a GC/MS study of Cadet's fuming liquid and an NMR investigation of the minor products to correct the bizarre structures that were proposed.

Relevant to the report of Valeur and Gailliot is a ^1H NMR study by Van Wazer and co-workers on the equilibria involving linear and cyclic arsenomethanes.[32] Even at room temperature, molecules of the $(CH_3As)_n$ family undergo exchange reaction in which As−As (but not C−As) bonds are broken and re-formed. In mixtures initially containing a relatively large proportion of $(CH_3)_2As{-}As(CH_3)_2$ with $(CH_3As)_n$ it was found that $(CH_3)_2As{-}As(CH_3)_2$ and cyclo-$(CH_3As)_5$ predominate at equilibrium. In the case of mixtures of $(CH_3)_2As{-}As(CH_3)_2$ and cyclo-$(CH_3As)_5$ in which the latter predominates, a red solid precipitated which could not be redissolved and which turned brown on standing. In view of these equilibria, a more reasonable possibility than **2** for the $(CH_3)_5As_3$ of Vaileur and Gailliot is the linear $(CH_3)_2As{-}As(CH_3){-}As(CH_3)_2$. Compound **1** remains a mystery. The X-ray crystal structures of both cyclo-$(CH_3As)_5$[33] and a purple arsenomethane polymer[34] have been reported, as has the structure of $(CH_3)_2As{-}As(CH_3)_2$.[35]

One might think, in view of the very nasty properties of Cadet's fuming liquid and the derived cacodyl compounds, that no large-scale applications of these arsenicals would have been sought and developed. However, during both World War I and World War II, organoarsenic-based chemical warfare agents were produced and, in World War I, actually used.[36,37] Among these were diphenylchloroarsine, ethyldichloroarsine, and Lewisite (a mixture of *cis*- and *trans*-$ClCH{=}CHAsCl_2$). Apparently, Cadet's fuming liquid also was considered (but never used). In Germany, during World War I, Fritz Haber's chemical warfare efforts at the Kaiser Wilhelm Institute in Berlin apparently involved some work with Cadet's fuming liquid.[37] In the United States, during World War II, processes for the continuous preparation of Cadet's fuming liquid were developed at Edgewood Arsenal[38] and the University of Illinois.[39,40] The latter process was an improvement over Cadet's, which had been used by all subsequent investigators, mostly without change, for almost 200 years. In the continuous process, a mixture of As_2O_3 and 75% acetic acid was passed over an alkali metal carbonate catalyst at ~300−400 °C in a slow stream of carbon dioxide. Yields of around 70% were obtained in contrast to the much lower yields (<17%) obtained with the usual Cadet procedure.

In more recent times, there has been some interest in the applications of tetramethyldiarsine (and, to a lesser extent, of $[(CH_3)_2As]_2O$), as a ligand in transition metal complexes. Usually Cadet's fuming liquid was not a source of these compounds used in such studies.

---

(38) Witten, B. U.S. Patent 2,531,487 (Nov. 28, 1950); *Chem. Abstr.* **1951**, *45*, 2799.

(39) Fuson, R. C.; Shive, W. *J. Am. Chem. Soc.* **1947**, *69*, 559.

(40) Fuson, R. C.; Shive, W. U.S. Patent 2,756,245 (July 14, 1956); *Chem. Abstr.* **1957**, *51*, 2020.

(41) For leading references see: Gupta, V. K.; Krannich, L. K.; Watkins, C. L. *Inorg. Chem.* **1986**, *25*, 2553.

(42) Kober, F. *Chem. Ztg.* **1981**, *105*, 199.

(43) Trenkle, A.; Vahrenkamp, H. *Chem. Ber.* **1981**, *114*, 1343.

(44) Gowik, P.; Klapötke, Th. *J. Organomet. Chem.* **1991**, *204*, 349.

(45) Hayter, R. C. *Inorg. Chem.* **1964,** *5*, 711.

(46) Chatt, J.; Thornton, D. A. *J. Chem. Soc.* **1964**, 1005.

(47) Cotton, F. A.; Webb, T. R. *Inorg. Chim. Acta* **1974**, *10*, 127.

(48) Röttinger, E.; Trenkle, A.; Müller, R.; Vahrenkamp, H. *Chem. Ber.* **1980**, *113*, 1280.

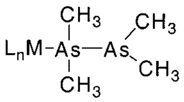
(49) Vahrenkamp, H.; Keller, E. *Chem. Ber.* **1979**, *112*, 1991.

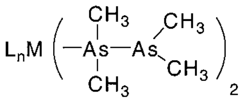
(50) Umland, P.; Vahrenkamp, H. *Chem. Ber.* **1977**, *110*, 2809.

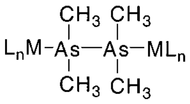
(51) Beurich, H.; Vahrenkamp, H. *Chem. Ber.* **1981**, *114*, 2542.

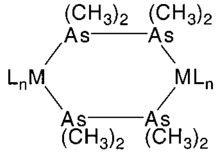
Rather, the availability of $(CH_3)_2AsCl$ and other dimethylarsino compounds by other routes made simpler syntheses possible.[41] For instance, the reaction of $(CH_3)_2AsH$ with $(CH_3)_2AsN(CH_3)_2$ in toluene at −10 °C gave tetramethyldiarsine in 76% yield.[41] Such preparations, carried out in an inert atomosphere box or in a Schlenk line, of course, were more easily and safely effected than in Bunsen's time.

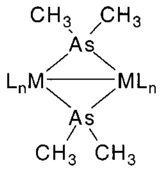
In principle, there are several ways in which $Me_2As-AsMe_2$ could react with transition metal complexes: (1) formation of monodentate complexes of types A and B; (2) formation of a bridged complex in which both arsenic atoms are coordinated to a metal center, types C and D; (3) with cleavage of the relatively weak As−As bond (dissociation energy ~38 kcal/mol in $Me_2As-AsMe_2$[42]) to form a bis(arsenido) complex (types E and F).

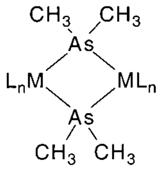

A


B

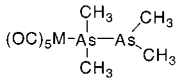
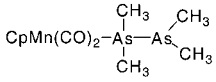
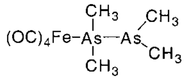
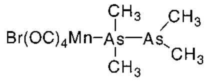
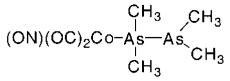
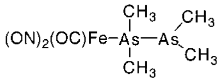
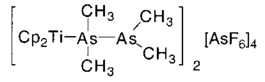

C


D

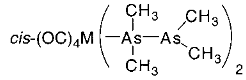

E

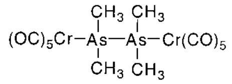
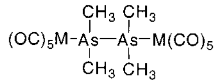
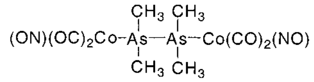
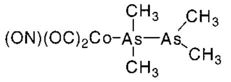

F

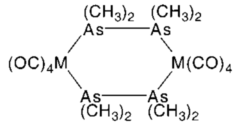
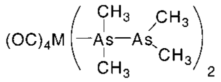
Selected examples follow below. All were prepared by the reaction of $(CH_3)_2As-As(CH_3)_2$ with the appropriate transition metal complex.

TYPE A		REF.
	M = Cr, Mo, W; *via* $M(CO)_5THF$	43
	*via* $CpMn(CO)_2THF$	43
	*via* $Fe(CO)_5$ in THF	43
	*via* $Br(OC)_5Mn$	43
	*via* $ON(OC)_3Co$	43
	*via* $(ON)_2(OC)_2Fe$	43
	*via* $Cp_2Ti(AsF_6)_2$	44

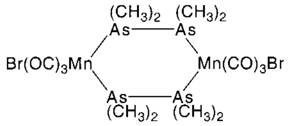
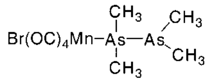
All the above $(CH_3)_4As_2$ complexes are very air-sensitive yellow to red oils.

TYPE B		REF.
	M = Cr, Mo, W, *via* $(OC)_4M(nbd)$ nbd = norbornadiene	43

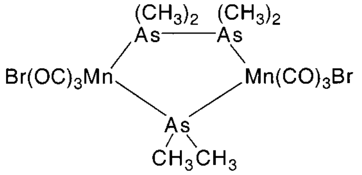
TYPE C		REF.
	*via* $Cr(CO)_6$ in refluxing hexane	45
	M = Mo, W; *via* $M(CO)_6$, no solvent at 200°C	46
	*via* thermolysis of 	43

TYPE D		REF.
	M = Cr, Mo, W; *via*  + $(OC)_4M(nbd)$	43

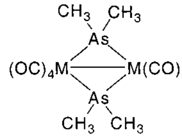
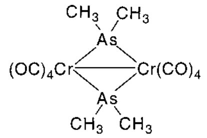
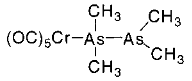
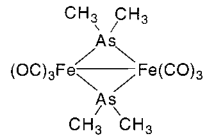
The Cr_2As_4 cyclic product also was produced in low yield in the reaction of cacodylic acid, $(CH_3)_2As(O)OH$, with $Cr(CO)_6$ in diglyme at 130 °C.[47]

	*via* thermal decomposition of 	48

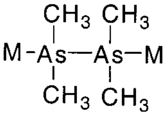
Thermolysis of the Mn_2As_4 cyclic complex above gave


48

The Cl analogue was prepared by warming the reaction product of $(OC)_5MnK + (CH_3)_2AsCl$ above −30 °C.[48]

TYPE E		REF.
	M = Mo, W; *via* $M(CO)_6$ in refluxing diglyme	45
	M = Mo, W; *via* $M(CO)_6$, sealed tube at 250°C	46
	*via* thermolysis at 220°C of 	49
	*via* $Fe(CO)_5$ at 180°C	46

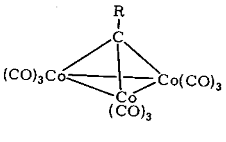
Tetramethyldiarsine complexes also have been obtained in reactions that did not involve the ligand as a starting material. In one example of this approach, dimethylarsine complexes, $M{-}As(CH_2)_2H$ ($M{=}Cr(CO)_5$, $Mo(CO)_5$, $W(CO)_5$, $Mn(CO)_4Cp$, $Fe(CO)_4$, $Fe(CO)(NO)_2$, $Co(CO)_2(NO)$, and $Ni(CO)_3$) were oxidized with air to the corresponding



$$\mathrm{M{-}\overset{CH_3}{\underset{CH_3}{As}}{-}\overset{CH_3}{\underset{CH_3}{As}}{-}M}$$

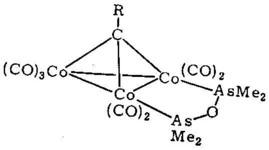
complexes of type C.

Cacodyl oxide also has served as a ligand in transition metal complexes. Reactions of the alkylidynetricobalt nonacarbonyl clusters **5** with $(CH_3)_2AsOAs(CH_3)_2$ in 1:1 molar ratio gave products of type **6** in good yield.[51] Reactions of the latter or of **5** with a 10-fold excess of cacodyl oxide gave CCo_3 clusters that contained two cacodyl oxide ligands, **7**. Use of an even greater 40-fold excess of cacodyl oxide and more forcing reaction conditions made possible the synthesis of clusters containing only three carbonyl ligands, **8** (with exception of the cluster with R = Cl, which was unstable). More complex byproducts were obtained in some of the 2:1 (**9**) and 3:1 (**10**) reactions when a sample of cacodyl oxide was used that had been stored for some time, i.e., which apparently had undergone some disportionation and whose ^1H NMR spectrum showed the presence of $(CH_3)_2AsOAs(CH_3)OAs(CH_3)_2$. No doubt much more coordination chemistry, of di- and polynuclear metal complexes in particular, using cacodyl oxide as ligand should be possible.

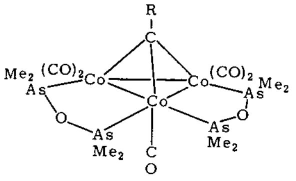


(R = H, CH_3, C_6H_5, CL)

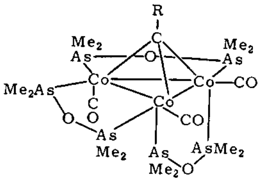
5



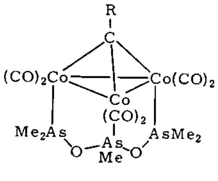
6



7

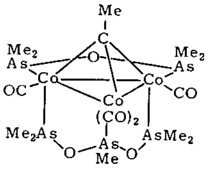


8



(R = Me, Ph)

9



10

Concluding Remarks

The components of Cadet's fuming liquid, as we have seen, have had a colorful history. They were discovered accidentally at a time when chemical knowledge was still rudimentary, before the experimental techniques needed to deal with such noxious, inflammable compounds were available. It was not until 80 years after their discovery that Robert Bunsen, a master experimentalist, took up their challenge and developed his "Bunsen ware", the forerunner of the Schlenk ware that we now use, to deal with them—a heroic effort that developed their chemistry but left important questions unanswered. Experiments of later workers provided further insight so that the constitution of the main components of Cadet's fuming liquid as $(CH_3)_2AsOAs(CH_3)_2$ and $(CH_3)_2As{-}As(CH_3)_2$ was established. However, the exact composition of Cadet's fuming liquid, while approximately known, still requires a careful investigation using modern procedures and instrumentation.

Because of its noxious, toxic properties, Cadet's fuming liquid has been considered for use as a chemical warfare agent and, despite them, its major components have been used in recent times as ligands in transition metal coordination chemistry. The inert atmosphere boxes, Schlenk lines, fume hoods, and ground glassware of today have made their preparation and handling fairly straightforward (provided one is careful!). Looking back, we must express our admiration for the early chemists who worked with them without these aids, who suffered their noxious odors and ill effects in the interests of science.

Acknowledgment. My thanks are due to Dr. Jean Escudié (Paul Sabatier University), Dr. Stephan Schulz (University of Bonn), Professor A. L. Rheingold (University of Delaware), and Professor R. H. Holm (Harvard University) for access to needed literature, to Dr. Escudié for some translations of French literature, and to my secretary, Ms. Colleen Rasmussen, for chasing down old literature in the bowels of the MIT libraries.

Dietmar Seyferth

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

OM0101947