# Perfume at the forefront of macrocyclic compound research: from Switzerland to Du Pont

Galina Shyndriayeva

King's College London, London, United Kingdom

A set of corporate publicity photographs from 1937 depicts several stages in the making and testing of perfumes, including one tableau of a perfume laboratory with a man and a woman sniffing smelling strips, and another depicting the "director of the perfume laboratories".[1] These photographs were not taken for a perfume house or an essential oil supplier; neither do they depict the workings of a firm in Grasse or Paris. These are instead portraying one line of business of the venerable giant of the American chemical industry, E.I. du Pont de Nemours & Company. From the 1930s into the postwar period, Du Pont manufactured and sold synthetic scents and aroma chemicals. While these chemicals were never important either in terms of output or revenue, their production by Du Pont is significant. One of these scents, a synthetic musk, was a direct product of Du Pont's famed Experimental Research Station, 'Purity Hall', an output of the research of Wallace Carothers and his group. In this paper I will argue that the study of perfume was a driver for research in organic chemistry in the twentieth century, particularly in investigations of macrocyclic compounds. This was possible because of the strong financial support given by the fragrance industry, which was willing to invest in expensive processes. After situating this claim in historiography, I will focus in particular on the scent of musk and its synthesis, tracing the research of Nobel Prize chemist Leopold Ruzicka as well as the continuation of his work by Wallace Carothers and his group.

Reflecting on the development of modern perfumery, Ruzicka asserted that "right from the earliest days of scientific chemistry up to the present time perfumes have substantially contributed to the development of organic chemistry as regards methods, systematic classification, and theory".[2] Such a statement seems astonishing considering how little attention has been given to perfumery in the study of academic and industrial chemical research. How did a Nobel Laureate come to make this claim? Did perfume indeed have an effect on the research questions of organic chemistry and if so, how?

In the historiography on the chemical industry, perfumery is given limited attention.[3] Insofar as it has been studied, it has been a story of the rise of synthetic chemistry in the late

[1] From the Aromatics-synthetic perfumes folder, Box 4, DuPont Company Product Information photographs (Accession 1972.341), Hagley Museum and Library, Wilmington, DE 19807.
[2] *Firmenich and Co: Successors to Chuit Naef and Co*, Geneva, 1895-1945. 1945. (Geneva: Firmenich). 38.
[3] For example it receives sparing mention in the general histories of Ihde, Aaron J, 1964, *The development of modern chemistry*, New York: Harper and Row, and Aftalion, Fred, 1991, *A History of the International Chemical Industry*, Otto Theodor Benfey, translator, Philadelphia: University of Pennsylvania Press, no attention in histories of firms which produced aroma chemicals such as Du Pont in Hounshell, David and John Smith, 1988, *Science and Corporate Strategy: Du Pont R&D 1902-1980*, Cambridge: Cambridge University Press, and no attention in more recent volumes on the European chemical industry such as Lesch, John E., ed, 2000, *The German Chemical Industry in the Twentieth Century*, Dordrecht: Kluwer.

nineteenth century.[4] Subsequent research into chemical products has received less consideration as though the twentieth-century development and use of these materials was an inexorable advancement given the breakthrough of the 1880s. This account is both invention-centric and does not seriously assess the perfume industry as part of the twentieth-century organic chemical industry and obscures its global connections.[5] The story of Carothers' work on scents is most thoroughly described in a couple of pages in Matthew Hermes' biography of Carothers.[6] Hermes, a professor of organic chemistry, clearly related the highlights of the Carothers group research, and noted that it was an extension of Ruzicka's findings, but treated this work as a small amusing episode in Carothers' career and did not further discuss Du Pont's perfume business or Ruzicka, nor make claims about the role of perfume in organic chemistry research. Hounshell and Smith also very briefly noted that Du Pont sold one of Carothers' synthetic compounds as a perfume ingredient but did not mention Ruzicka's work as foundational.[7] Similarly, Ruzicka's work on fragrances has only been examined in his biography, by the historian Gerhard Oberkofler, and mentioned in short biographies written by chemists working in the perfume industry, the most important of which is the Royal Society biographical memoir written by Ruzicka's former students and colleagues Vladimir Prelog and Oskar Jeger.[8] These two works do give due attention to Ruzicka's collaboration with the perfume industry and I will be reliant on them for my analysis of Ruzicka's work; however they do not discuss the continuation of his work by Du Pont. Additionally, I will be supplementing my discussion of Ruzicka's research with primary material from oral interviews and scientific publications.

## Perfume in industrial research: Switzerland

One reason for the importance of perfumes to organic chemistry is that perfumes were complex substances, but ones it was very well worthwhile making synthetically if possible. They were expensive and rare.[9] For example, musk was a subject of dedicated study among academically-trained chemists from the 1880s; natural musk is one of the most expensive materials used in perfumery. While one was not reliant on chance to obtain it, as for ambergris, it did involve the hunting of musk deer for their fragrant pouches in Tibet, China, Assam, Nepal and Russia. 30-50 deer were sacrificed for a kilogram of musk.[10] The first suitable synthetic musk substitute however was a chance product, a result of Albert Baur's

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[4] Recent historiography of cosmetics and perfumery has focused on the nineteenth century and the French case, without deeply engaging with the history of chemistry. For example, see: Briot. Eugénie. 2008. *La chimie des élégances : La parfumerie parisienne au XIXe siècle, naissance d'une industrie du luxe*. (Conservatoire National des Arts et Métiers, Centre d'Histoire des Techniques et de l'Environnement).

[5] This claim builds on Geoffrey Jones' work (Jones, Geoffrey. 2010. *Beauty Imagined: A History of the Global Beauty Industry*. [Oxford: Oxford University Press]).

[6] Hermes, Matthew E. 1996. *Enough for one lifetime: Wallace Carothers, inventor of Nylon*. (Washington, D.C.: American Chemical Society and the Chemical Heritage Foundation).

[7] Hounshell and Smith (note 3): 243.

[8] Oberkofler, Gerhard. 2001. *Leopold Ruzicka, 1887-1976: schweizer Chemiker und Humanist aus Altösterreich*. (Innsbruck: Studien Verlag).
Prelog, Vladimir and Jeger, Oskar. 1980. Leopold Ruzicka. 13 September 1887-26 September 1976. *Biographical Memoirs of Fellows of the Royal Society*, **26**: 411-501.

[9] In this a parallel can be drawn with natural, expensive dyes and the history of synthetic dyes.

[10] Kraft, Philip. 2005. Aroma Chemicals IV: Musks: 143. In: *Chemistry and Technology of Flavors and Fragrances*. David Rowe, ed. (Oxford: Blackwell): 143-168.

experiments with explosives in 1888. In 1906 it was a chemist in Leipzig at the fragrance company Schimmel (a firm which invested extensively in the creation of an industrial centre for perfume materials research) who isolated the main compound for musk's odour, a macrocyclic compound.[11] Heinrich Walbaum also identified the compound as a ketone, named it muscone and derived its empirical formula.[12] Civetone, a musk odour compound from the civet cat, was also identified as a ketone and isolated in 1915 by E. Sack.

It was with Chuit and Naef that Ruzicka would continue the research of Heinrich Walbaum. Chuit and Naef, with whom Ruzicka would remain involved throughout his career, was founded by a businessman, Martin Naef, and a chemist, Philippe Chuit, in 1898. Chuit studied chemistry with Carl Graebe in Geneva and Henri Brunner in Lausanne and worked for Sandoz in Basel; thus he was firmly inscribed in the Swiss chemical industry.[13]

Industry was not Ruzicka's first choice.[14] He had completed his doctorate in 1910 at the Technische Hochschule in Karlsruhe under Hermann Staudinger, and afterwards worked as Staudinger's assistant in Zurich when the former was appointed Professor and Chair of the Department of Chemistry at the ETH (Eidgenössische Technische Hochschule/Swiss Federal Institute of Technology) in 1912.[15] Staudinger was awarded a Nobel Prize in chemistry in 1953 for his demonstration of the existence of polymers, large molecules composed of repeating subunits, and subsequent work.[16] In was in his postdoctoral work with Staudinger from 1911-1916 that Ruzicka embarked upon the field of study which would become his lifetime career, natural product chemistry and terpenes.[17] Staudinger and Ruzicka isolated and determined the structure of pyrethrins, insecticidal compounds found in certain species of daisy, including one of Dalmatian origin, such as *Chrysanthemum cinerariifolium, Tanacetum cinerariifolium* and *Chrysanthemum coccineum*. The pyrethrins are of a class of compounds called terpenoids, multicyclic chemicals similar to terpenes. Extracted pyrethrins and the synthetic analogues, pyrethroids, continue to be important insecticides. Ruzicka's first independent work continued the focus on natural terpenes, which would be foundational for his later work in the perfume industry as a number of fragrant compounds are terpenes. He performed the synthesis of a fragrant ketone called fenchone, a component of fennel oil and some leaf oils. He completed a synthesis of linalool in 1919 and of α-pinene in 1921.

[11] These macrocyclic molecules should be distinguished from polycyclics; macrocyclic substances are composed of one large many-membered ring, while polycyclic molecules are composed or two or more rings. While muscone and Du Pont's musk Astrotone are macrocyclic, a number of synthetic musks from the 1950s onwards are polycyclic, including International Flavors and Fragrances' Galaxolide, the synthetic most widely used in the early twenty-first century. Kraft (note 10): 147, 152-155.
[12] Walbaum, H. Das natürliche Moschusaroma. *Journal für praktische Chemie.*: **73**, 488–493.
[13] Oberkofler (note 8): 61.
[14] Oberkofler saw Ruzicka as emotionally attached to academia. Oberkofler (note 8): 63.
[15] Leopold Ruzicka (1887-1976) was born in the Austo-Hungarian Empire, in Vukovar, Croatia. At Karlsruhe he was also taught by Fritz Haber and completed both an Engineering Diploma and a doctorate studying ketenes under Staudinger. Prelog and Jeger (note 8): 411- 412.
[16] For a study of Staudinger's career and the foundation of polymer studies, see Yasu Furukawa's 1998 work: *Inventing Polymer Science: Staudinger, Carothers and the Emergence of Macromolecular Chemistry*. (Philadelphia: University of Philadelphia Press).
[17] Prelog and Jeger (note 8): 412. Terpenes are a class of compounds very important in natural products; they consist of arrangements of isoprene units. Isoprene is a hydrocarbon of the formula $C_5H_8$, with the IUPAC name 2-methyl-1,3-butadiene.

Staudinger curtailed continued support when Ruzicka expressed his intention to work on more independent projects and so at an early stage in his career the latter was obliged to seek outside financial assistance to develop his own line of research.[18] Ruzicka's first industrial contact, Haarmann and Reimer was established in Holzminden, Germany in 1874, by chemists who had trained under Hofmann in Berlin, to manufacture synthetic vanillin. However Ruzicka's first project on fragrance materials was unsuccessful; in his period of work for Haarmann and Reimer, 1917-1920, he was unable to synthesise irone, an aroma chemical of violet. However, the project allowed Ruzicka to become more experienced with a certain type of structural change occurring in chemical reactions, a rearrangement of atoms called the Wagner-Meerwein rearrangement, which would be foundational for his future work.[19]

Ruzicka had been in contact with Chuit and Naef in 1919, but did not agree to undertake direction of research until January 1921, beginning "a highly propitious and productive symbiosis".[20] From the start Chuit and Ruzicka worked together closely, and together compiled a list of six interesting molecules to investigate, that is, to determine structures and synthesise possible substitutes, as a research programme: nerolidol, jasmone, farnesol, irone, civetone and muscone.[21] Ruzicka's choice of industrial partners indicates the status of perfumery as a scientific industry, a viable partner not only for funding and temporary projects but for sustained research.

From the funding allotted by Chuit and Naef, Ruzicka hired assistants. While he did not receive funding from the ETH, he did hold honorary appointments of Privatdozent from 1918 and Titular Professor from 1923, so that he was able to have his own students and space. Ruzicka and his group only worked on-site at the Geneva laboratories of Chuit and Naef for a year from March 1925, when relations with Staudinger became strained.[22] In 1927, Ruzicka obtained an academic position at the University of Utrecht, but continued to maintain a close relationship with Chuit and Naef during his career.

The chemistry of terpenes as well as macrocyclic compounds was not trivial and the list of molecules which Chuit and Ruzicka agreed upon was not lacking in ambition; Ruzicka promised Martin Naef, "For the first time we have before us a rare chance to do something really novel in perfume chemistry."[23] Macrocyclic compounds such as muscone were considered to be very unstable and impossible to synthesise, based on Adolf von Baeyer's strain theory, and carbon rings of more than eight carbons had not yet been identified.[24] However, Ruzicka's series of papers in 1926 based on work he had begun a few years earlier with Chuit and Naef countered that understanding. He elucidated the structure of civetone to

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[18] Prelog and Jeger (note 8): 413.
[19] Prelog and Jeger (note 8): 413, 428.
[20] Prelog and Jeger (note 8): 413.
[21] Oberkofler (note 8): 61-62. Chuit proposed the same list, but with nerol for nerolidol. The compounds are components of a number of essential oils, but the predominant origin is as follows: nerolidol from orange blossom oil, jasmone from jasmine, farnesol from acacia blossoms, and irone from iris essential oil.
[22] Ruzicka was also Privatdozent at the University of Zurich from 1920. Prelog and Jeger (note 8): 413-414; Oberkofler (note 8): 62.
[23] Cited in Prelog and Jeger (note 8): 425.
[24] Prelog and Jeger (note 8): 413, 425.

be a large ring and then conjectured that muscone must also be of a similar structure before experimental confirmation.[25] In synthesis experiments, he was able to identify a reaction which produced large-ringed ketones and synthesised a series of these compounds from 9 to 29 carbons, of which the 14-18 membered rings had the strongest musk odour. The reaction was dry distillation of thorium and cerium salts of certain dicarboxylic acids. Chuit and Naef were most likely quite pleased with these results, as one of the rings was successfully marketed: cyclopentadecanone/*nor*-muscone with the trade name Exaltone. This was almost identical to natural musk but was missing a methyl ($CH_3$) group.[26] Ruzicka then embarked on a study of related macrocyclic compounds, ketones, lactones, ketoximes, lactams, imines, amines and alcohols produced through various steps of reduction, oxidation and rearrangements, to determine general properties and stereochemistry and develop theoretical insights into large rings and multi-ringed compounds. Ruzicka showed that large ring compounds could exist, were not subject to a special strain and indeed could have lower heats of combustion than small rings.[27]

The commercial import of the work on musks is evidenced by the competition to release a synthetic to market. For example, Haarmann and Reimer, a strong competitor against Chuit and Naef, strove to gain a market in musk substitutes. In 1927 one of their researchers, Max Kerschbaum, isolated a vegetal musk, a macrocyclic lactone identified as 15-pentadecanolide, from Angelica root oil.[28] However Chuit and Naef were first to be able to produce the molecule on an industrial scale, branding it Exaltolide®.[29] It was synthesised by an oxidation step (a Baeyer-Villiger reaction) from Ruzicka's first commercial musk for Chuit and Naef, Exaltone. Kerschbaum also isolated another vegetal musk, ambrettolide from Ambrette seed oil, which Haarmann and Reimer were able to sell, synthesising it from shellac.[30]

Ruzicka's work on terpenes continued in earnest at Chuit and Naef with studies into synthesising farnesol and determining the structure of and synthesising nerolidol. Many terpenes important in perfume are sesquiterpenes, which are composed of three isoprene units, of which farnesol and nerolidol are examples. As Prelog and Jeger noted, the "interest in this field was by no means pecuniary."[31] When Ruzicka began work on the sesquiterpenes, there was scant understanding of their structure and no sesquiterpene found in nature had yet been synthesised. He developed a different procedure to determine structure and satisfied the latter with synthesis of nerolidol. Building on the work of German chemist and Nobel laureate in Chemistry (1910) OttoWallach, Ruzicka found further evidence for three isoprene units as the structure of sesquiterpenes.[32] Ruzicka continued work on sesquiterpenes after returning to academic positions both at Utrecht and Zurich, especially in the late 1920s and 30s but also

[25] Prelog and Jeger (note 8): 431.
[26] It was later identified to be a naturally-occurring compound in the scent gland of the Louisiana muskrat. Kraft (note 10): 146.
[27] Prelog and Jeger (note 8): 425. Specifically, heats of combustion per methylene group of 15- and 30-member hydrocarbon rings (cycloalkanes) were lower than for cyclohexane and cyclopentane.
[28] Kerschbaum also determined the structure of farnesol in 1913, one of the compounds Ruzicka worked to synthesise at Chuit and Naef. Prelog and Jeger (note 8): 437.
[29] Kraft (note 10): 147.
[30] Kraft (note 10): 147, 149.
[31] Prelog and Jeger (note 8): 437.
[32] Prelog and Jeger (note 8): 437-438.

into the 1950s, working on constituents of such natural products as the oils of sandalwood, eucalyptus, celery and clover.

The fragrance industry was a very propitious site for investigating this complicated chemistry as it was able to gain favourable margins on its products and thus supply a large amount of financial support for these experiments. The reaction yields of Ruzicka's musks were very low, from 0.1% to 6%, but though the reactions were expensive these were still very profitable in the musks market where a kilogram of muscone cost 300,000 Swiss francs.[33] Chuit and Naef's financial backing allowed Ruzicka to build a research group, some members of which made their careers in perfume-related research and moved between industry and academia, such as Max Stoll and Hans Schinz. Max Stoll remained at Chuit and Naef (to be renamed Firmenich in 1934) as head of research from 1927 when Ruzicka left Geneva to continue his work on terpenes and macrocyclic compounds as Chair of Organic Chemistry at the University of Utrecht.[34] Hans Schinz joined Ruzicka at the ETH and had doctoral students of his own, one of whom was Albert Eschenmoser, who completed his thesis on sesquiterpene chemistry and later synthesised vitamin $B_{12}$ in collaboration with Harvard.[35] Chuit and Naef's later incarnation as Firmenich continued to heavily support the work of Ruzicka's team; Eschenmoser, who remained a consultant for them, remembered that "For many years they [both Firmenich and CIBA] have supported my group very generously, without any strings attached," their funding "was very important for us."[36]

Ruzicka's study into chemically interesting fragrance molecules led him to consider research questions in the wider field of terpenes and terpenoids then into steroids and hormones, as Prelog and Jeger attested. One of Ruzicka's major contributions to the chemistry of terpenes was his establishment of the Isoprene Rule, a proposal made by Otto Wallach in 1887 but not considered significant. It was thus Ruzicka's work for a perfume company which provided much of the impetus and the foundation for his Nobel-Prize winning research.

**Perfume in industrial research: the Du Pont Experimental Station**

Moving from the laboratories of a small but profitable Swiss synthetics firm, Ruzicka's research was taken up by the chemists of the largest chemical company in the United States, Du Pont.

Following the *mensis mirabilis*, as Hounshell and Smith labelled April of 1930, the Carothers group delved more deeply into the theoretical consequences and new avenues posited by their accomplishments of the synthesis of neoprene and a laboratory-made polyester fibre, one avenue of which, namely further studies into polymerisation, led to the synthesis of fragrant macrocyclic molecules. From the late 1920s Carothers had been working on synthesising substances of high molecular weight, higher than previous successes – these substances were

[33] Prelog and Jeger (note 8): 425.
[34] Prelog and Jeger (note 8): 414. Ruzicka returned to ETH when he was hired as Chair in 1929, after the previous Chair, Richard Kuhn, left for the Kaiser Wilhelm Institute for Medicinal Chemistry in Heidelberg.
[35] Oral history interview with Albert Eschenmoser, 1985, Chemical Heritage Foundation: 6-7.
[36] Eschenmoser (note 25): 30.

polymers, synthesised through a process of polymerisation.[37] Carothers published a series of papers in the *Journal of the American Chemical Society* presenting his group's work on polymerisation. As noted above, polymerisation was a very active field of study in the 1920s, though in a "disorganised" state before the formulation of Carothers' theory, according to organic chemist Roger Adams.[38]

In 1932, Carothers together with Julian W. Hill developed a research project on cyclic molecules. Hill was the member of Carothers' group sharing responsibility for the linear condensation polymers/synthetic fibre synthesis. Condensation reactions, where water is released as a by-product of a reaction (in this case the functional groups of two or more substances react and result in covalent bonds), were the group's primary means of building polymers. In his project to build high-weight polyester chains, Hill facilitated the synthesis by realising that a molecular still could overcome the current impediment – Carothers conjectured that water formed during polyester reactions hindered formation of longer chains and needed to be removed. The still could be used to trap and remove the water.[39] The still did indeed lead to the formation of polymers of much higher molecular weight and subsequently was also decisive in the synthesis of aroma chemicals. Specific aroma chemicals, of a large-ring macrocyclic structure, became of great interest to Carothers and Hill as these molecules exist in equilibrium between ring and long-chain polymer forms.

Ruzicka's research was the foundation for Hill and Carothers' work; no one outside his group had yet taken Ruzicka's "finished and very striking researches on the constitution of the musks" further.[40] Carothers was very deliberate in his intention to develop the field of macrocyclic molecules.[41] The standard set-up for a polymerisation reaction was between dibasic (diprotic) acids and glycols. The Du Pont researchers proceeded to try a series of synthetic reactions, systematically making macrocyclic compounds of increasing size in as many combinations of various dibasic acids and glycols as available. Hill recollected that musky odours were detected in almost any combination of glycols and acids, as long as the ring was within a certain size.[42] Already by July of 1932, Carothers reported that these molecules could be commercialised as "substitutes for one of the most costly type of perfume materials."[43] Among the different series, the most powerful odour came from a reaction with the hexamethylene glycol. Another researcher, Frank J. Van Natta, was conducting the reactions, presuming that the crystalline substance deposited on his apparatus was distilled excess glycol; Hill recollects himself realising that the substance was probably a large ring, cyclic hexamethylene carbonate, which resulted in a camphoraceous odour.[44] Based on

[37] For a detailed account of Carothers' polymer research, see Furukawa (note 16) and Hounshell and Smith (note 3): 223-248.
[38] Adams, Roger. 1939. Biographical Memoir of Wallace Hume Carothers. *National Academy of Sciences, Biographical Memoirs* **20**: 301.
[39] Furukawa (note 16): 136-138; Hounshell and Smith (note 3): 236-237.
[40] 14 January 1930, Carothers to Charles Stine. Accession 1784, Box 18, Hagley Museum and Library, Wilmington, DE 19807.
[41] Oral history interview with Julian Hill, 1982, Hounshell and Smith oral history interviews, 1982-1988, Accession 1878, Hagley Museum and Library: 33.
[42] Hill (note 41): 36.
[43] July 1932 report: 4. Accession 1784, Box 18, Hagley Museum and Library.
[44] Hill (note 41): 35.

Ruzicka's research, larger rings synthesised from larger molecules of methylene carbonate would be predicted to have a musk odour. Hill himself performed the synthesis using the larger glycol tetradecamethylene, which yielded the very musky tetradecamethylene carbonate.[45] By August 1933 the group had not yet succeeded in isolating the compounds, but Carothers sent samples of the pungent products to Bolton and Stine. Bolton was apparently ready to dismiss the project as a 'hoax'.[46]

The work on large rings was very fruitful for Carothers and his colleagues. Julian Hill's letter nominating Carothers for the American Chemical Society's William H. Nichols Medal in 1934 enumerates the outcomes of the research as: new method of synthesising many-membered cyclic compounds, several new types synthesised, and new data for studying and conceptualising ring formation.[47]

Tetradecamethylene carbonate was the original Astrotone, Du Pont's commercial synthetic musk. It was first introduced as a synthetic musk in the 1933 meeting of the American Chemical Society and described in the Carothers publication series on polymers. The trade name Astrotone was announced in the November 1934 issue of Du Pont Magazine, and was available for purchase at $200 per pound. The Purity Hall musk was further developed for marketable production by another member of the Carothers group, Edgar Spanagel. Indeed, when he joined Du Pont in 1933, on his first day of work Spanagel was assigned to the on-going perfume project.[48] This project was recently expanded through sponsorship from the Organic Chemicals Department (Orchem), to determine whether any of the cyclic molecules could be viable on a larger scale. Orchem decided that tetradecamethylene carbonate was the only promising compound at that time.[49] Spanagel was put to task on optimising the synthesis of the musky macromolecules, specifically a 17-member ring, as yields were very small and inconsistent. After maintaining at a specific pressure the vacuum in which the starting polymer was heated, Spanagel recalled that the macrocyclic compound was produced consistently and yielded as much as 100 grams per batch.[50] Spanagel then travelled to the Organic Chemical plant in New Brunswick, New Jersey to work on further streamlining the reactions and preparation of intermediate reagents.[51] From November 1933, Spanagel was suspended from direct work on tetradecamethylene carbonate until Orchem would decide that manufacturing would be undertaken, but continued to work on cyclic molecules.

[45] Hill (note 41): 35.
[46] Hill (note 41): 35.
[47] Julian Hill to J.M. Weiss, 28 August 1934, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[48] Oral history interview with Edgar W. Spanagel, 1997, Chemical Heritage Foundation: 9.
[49] Carothers to Bolton, New Project on Substituted Bifunctional Esters, 10 November 1933, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[50] Spanagel (note 48): 9 -10; Carothers to Bolton, New Project on Substituted Bifunctional Esters, 10 November 1933, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[51] Carothers to Bolton, New Project on Substituted Bifunctional Esters, 10 November 1933, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.

However, what is now known as Astrotone is a molecule called ethylene brassylate, synthesised by Spanagel. In the search for a range of different glycols and dibasic acids as starting materials for polymerisation, Carothers asked a colleague at Cornell, John R. Johnson in May 1932, whether the ozonisation methods he was developing could produce a good yield of higher weight dibasic acids.[52] Johnson sent the directions for production of the compound his group had found interesting, dimethyl brassylate. Spanagel then worked on the ring formation with this compound and produced ethylene brassylate, a 17-member ring with a strong musk odour, using tin chloride as a catalyst.[53] Spanagel's patent including this synthesis covered the more general ground of preparing cyclic esters of 7 or more members, using catalysts he determined were effective, of which tin chloride is one type.[54] From the 37 new cyclic esters listed in his patent, he used three as examples of musk or civet substitutes, suggesting that those with 15-17 member rings were most suitable: ethylene brassylate, nonamethylene adipate and hexamethylene azelate. According to Spanagel, ethylene brassylate was much easier to make than tetradecamethylene carbonate, especially with the catalysts described in his patent, and so perhaps for this reason was the more successful commercial Astrotone.[55] The tetradecamethylene carbonate Astrotone was made by Orchem for a brief period. According to Merlin Brubaker's account of the laboratory legend, 300 pounds of tetradecamethylene carbonate were produced, but Orchem was unable to sell it until a Rhone-Poulenc representative evinced interest. Rhone-Poulenc then resold "for some fabulous price" after diluting it by fifty percent and adding diethylamine, a strongly unpleasant smelling compound, which measures seem to have proved beneficial as it was then allegedly used in a successful French perfume.[56]

The Carothers group perfume project was a small but vibrant part of Du Pont's fundamental research section. Apart from the macromolecules, Hill, Brubaker and Carothers also worked on smaller questions such as substitution for perfume intermediates.[57] It incurred little expenditure compared to other projects, $7,484 in 1933 and less costs thereafter.[58] Projects continued until 1938, such as research on derivative of pinene and camphor in 1937, and condensation of terpenes with phenols in 1937 and 1938. The number of scientists involved was sizeable, Carothers and two of his colleagues, Julian Hill and Edgar Spanagel.

In conclusion, perfume materials were not only of commercial interest to companies, but certain compounds were of high chemical interest in the academy, as evidenced by the work of Ruzicka. The chemistry of these compounds was not ordinary or trivial, but was situated in

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[52] Carothers to Johnson, 24 May 1932, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[53] Hill (note 41): 36.
[54] Edgar W. Spanagel, 'Process of Preparing Cyclic Esters', US 2092031, 1937.
[55] Spanagel (note 48): 11; Hermes (note 6): 165.
[56] Oral history interview with Merlin Brubaker, 1982, Hounshell and Smith oral history interviews, 1982-1988, Accession 1878, Hagley Museum and Library: 20.
[57] E.g. o-toluic acid for benzoic acid. 8 August 1934, Paul Austin to Carothers, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[58] Fundamental Research Expenditure. Perfume Chemicals, Account S-1408-B-2, project number 1635, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.

the field flourishing at the time, polymer chemistry, and study of these compounds led to new insights in polymerisation and understanding of macrocyclic molecules, as seen also in Carothers' research.