# A Prelude to Biogermylene Chemistry

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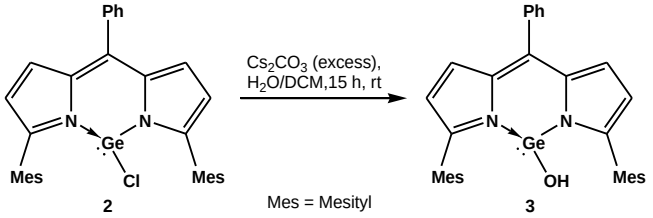
**Abstract:** The biological applications of germylenes remain an unconceivable domain owing to their unstable nature. We report the isolation of air, water, and culture-medium stable germylene DPMGeOH (**3**) and its potential biological application (DPM = dipyrromethene ligand). Compound **3** exhibits antiproliferative effects comparable to that of cisplatin in human cancer cells. The cytotoxicity of compound **3** on normal epithelial cells is minimal and is similar to that of the currently used anti-cancer drugs. These findings provide a framework for a plethora of biological studies using germylenes and have important implications for low-valent main group chemistry.

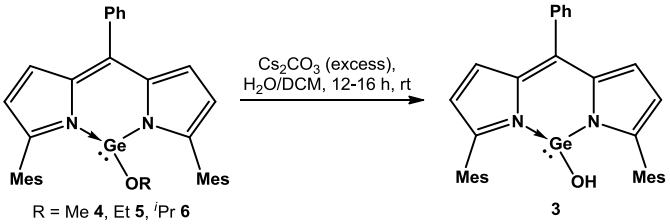
Several anti-cancer drugs are used for chemotherapy. Cisplatin, carboplatin, and oxaliplatin are platinum-based chemotherapeutic agents.[1] Organic compounds, such as doxorubicin, are also used in chemotherapy.[2] The adverse side effects and resistance of cancer cells to chemotherapy necessitate the development of new anti-cancer drugs.[1-5] Significant efforts are underway to synthesize and screen compounds with potential antiproliferative properties.[1-5] Metal complexes containing metal centers, such as titanium(IV), rhenium(I/IV), ruthenium(II/III), osmium(II), palladium(II), copper(I/II), gold(I/III), gallium(III), and bismuth(III) are being studied for their anti-cancer properties.[3] Among compounds with heavier group 14 elements, some tin(IV) compounds have shown anti-cancer properties, but undesired effects associated with these compounds limit their potential use.[4] Germanium(IV) compounds have also been screened for their anti-tumor activity [5] and germylenes have never been studied.[6] Germylenes are compounds containing Ge(II) centers with a lone pair of electrons on the germanium atoms.[6] They are the heavier analogs of carbenes (divalent carbon compounds) and are very reactive.[6] Almost all the germylenes require an inert atmosphere for stability.[6] Traditionally, germylenes are used as precursors to access other important germanium compounds,[6-7] and recently, they have been used as catalysts[8], small molecule activators[9], and precursors in materials chemistry[10]. For a compound to be useful for biological studies, it should be air, water, and culture-medium stable. No germylene has all these qualities; as a consequence, the biological properties of this group of compounds remain unknown. Here, we report the isolation of a novel germylene DPMGeOH (**3**) (Scheme 1), which is stable (vide infra) in air, water, and also in the culture medium [Dulbecco's Modified Eagle's Medium (DMEM); see Table S1 in the Supporting Information (SI)]. The isolation of compound **3** has provided us a chance to study the applications of germylenes in biology. In this communication, we narrate the (a) synthesis and characterization of germylene **3**, (b) antiproliferative effect of compound **3** on human cancer cell lines, and (c) benign nature of compound **3** towards normal epithelial cells (Vero cells), Gram-positive bacteria, and Gram-negative bacteria.

To synthesize germylene **3**, two simple synthetic methodologies that work entirely under atmospheric conditions were formulated. In the first route, addition of an excess of cesium carbonate dissolved in water to a solution of chlorogermylene DPMGeCl (**2**)[11] in dichloromethane (DCM) at room temperature gave germylene **3** as a reddish-orange solid in 85% yield (Scheme 1) (see the Experimental section in the SI). An excess of the base is essential, and its stoichiometric use leads to an incomplete reaction.




**Scheme 1.** Synthesis of germylene **3** from chlorogermylene **2**.

The chlorogermylene **2** was obtained through the reaction of DPMLi (the lithium salt of dipyrromethene DPMH (**1**)) with $GeCl_2$·(1,4-dioxane) at -78 °C in toluene (Scheme S1; see SI). As a second route, it was found that alkoxygermylenes **4**-**6** can react with water in the presence of cesium carbonate to provide germylene **3** in about 90% yields (Scheme 2). Alkoxygermylenes **4**, **5**, and **6** were synthesized through the reaction of compound **2** with alcohols (MeOH, EtOH, and $^i$PrOH, respectively) in the presence of cesium carbonate (Scheme S2; see SI).[13]




**Scheme 2.** Synthesis of germylene **3** from alkoxygermylenes **4**-**6**.

Though a large number of germylenes are known,[6-11] only two free hydroxygermylenes LGeOH (**I**)[12a] [L = CH{(CMe)(2,6-$^i$Pr$_2$C$_6$H$_3$N)}$_2$] and L$^1$GeOH (**II**)[12b] [L$^1$ = (2,6-$^i$Pr$_2$C$_6$H$_3$)NC(Ph)C(CH$_2$)$_4$CN(2,6-$^i$Pr$_2$C$_6$H$_3$)] are known (with stability under inert conditions), highlighting the significance of the hydroxygermylene **3** which is stable in air, water, and also in the culture medium. The air, water, and culture-medium stabilities of compound **3** were monitored by $^1$H NMR spectroscopy; it is stable for 10, 5, and 5 days, respectively (Figures S1, S2, and S3; see SI). It is anticipated that the stability of germylene **3** is due to the precise electronic stabilization and steric protection offered by the dipyrrinate ligand with mesityl groups to the low-valent germanium center. Further, to understand the reason behind the unique stability of compound **3**, we performed quantum mechanical calculations at the DFT level of theory using Gaussian 09 (see SI); the molecular orbital calculations were carried out with implicit solvent of water dielectric as a polarizable continuum model (PCM). As the composition of the frontier orbitals correlates with the reactivity, we analyzed the nature of the HOMO of compound **3** along with those of compounds **I** and **II**. A significant

difference was observed; HOMO is primarily located at the germanium atom in compounds **I** and **II**, whereas the contribution of the germanium atom to the HOMO is almost negligible in compound **3** (Figure 1). This aspect explains the air- and water-stability of compound **3** against that of the compounds **I** and **II**. As there was no germanium contribution to the HOMO of compound **3**, we also analyzed its HOMO-1 composition. It was found that (a) HOMO-1 has a major contribution from the germanium atom, and (b) the energy gap between the HOMO and HOMO-1 is not that high (5.1 kcal/mol). This low energy gap, as well as the presence of germanium contribution to the HOMO-1, support its slow decomposition to the free ligand (DPMH) over a long-standing in the aqueous medium (vide supra).

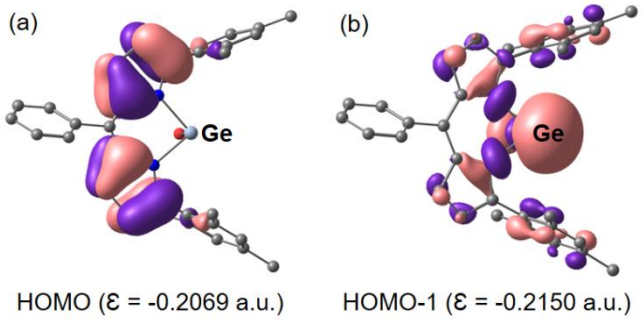



**Figure 1**. The HOMO (**a**) and HOMO-1 (**b**) of compound **3**.

Compound **3** is freely soluble in toluene, tetrahydrofuran, chloroform, and dichloromethane. It was characterized by various spectroscopic techniques, such as $^{1}H$ and $^{13}C$ NMR spectroscopy along with compounds **2** and **4**-**6** (Figures S4-S15 and Figures S19-S20; see SI). In the $^{1}H$ NMR spectrum of compound **3**, the OH proton resonates at 1.20 ppm. The IR spectrum of compound **3** showed a stretching band for the OH group at 3627 $cm^{-1}$ (Figure S20; see SI). Further, the molecular structure of compound **3** (Figure 2) was confirmed by single-crystal X-ray diffraction studies (see SI) together with compounds **2** (Figure S21; see SI) and **4** (Figure S22; see SI).

The stability of compound **3** offered a unique opportunity to assess the potential biological functions of germylenes. For the biological studies, the solution of compound **3** in DMSO was used. Though compound **3** has limited solubility in DMSO, it has adequate solubility required for the cell experiments. We studied the effect of compound **3** on the cell proliferation of HeLa, MCF7, and Huh7 cells using the MTT assay. For the comparison of cytotoxicity results, chemotherapeutic agents cisplatin and doxorubicin were also tested along with compound **3**. Cells were exposed to increasing concentrations of compound **3**, cisplatin, and doxorubicin for 24 hours, and their effect on cell proliferation was examined (Figure 3). Cells treated with DMSO were used as controls. As shown in Figure 3, compound **3** suppressed the cellular proliferation of HeLa [Figure 3(a)], MCF7 [Figure 3(b)], and Huh7 [Figure 3(c)] cells in a dose-dependent manner. Cell viability reduced significantly in these cells in comparison to that in the controls as the concentration of compound **3** increased from 0.5 $\mu$M to 25 $\mu$M.

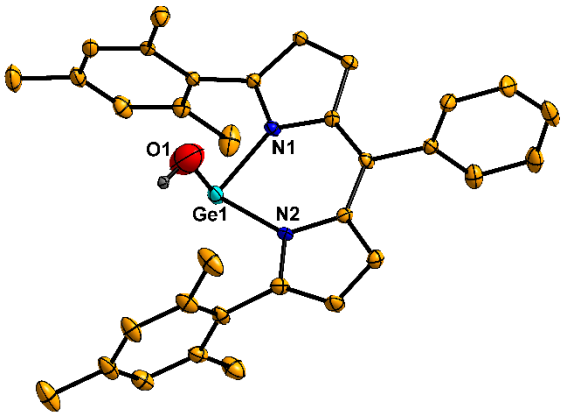



**Figure 2**. Molecular structure of compound **3**. All hydrogen atoms except that of the hydroxyl group are omitted for clarity, and thermal ellipsoids are drawn at the 30% probability level. Data collection temperature: 100 K.

The antiproliferative effects of compound **3** are marginally better than those of cisplatin in MCF7 and Huh7 cells [Figures 3(b) and 3(c)]. On HeLa cells, the antiproliferative effects of compound **3** are almost comparable to those of cisplatin [Figure 3(a)]. Doxorubicin had the most substantial antiproliferative effect on all the three cell lines studied [Figures 3(a) to 3(c)]. Comparable results for cell viability (a loss of about two-thirds of cell viability) were observed at 25 $\mu$M and 10 $\mu$M concentrations of compound **3** in HeLa and Huh7 cells, respectively (i.e., approximately a three-fold difference in the concentration of compound **3**). These findings reveal the existence of cell-type dependent differences in the susceptibility to germylene **3**. Trypan blue experiments for cell viability corroborated the findings on germylene-mediated suppression of cell proliferation (Figure S24; see SI). In addition, the colony formation assay was performed to determine the long-term inhibitory effects of germylene **3** on the proliferation of HeLa, MCF7, and Huh7 cells (Figure 4 and Figure S25 (see SI)). The results show that compound **3** significantly inhibits colony formation in HeLa, MCF7, and Huh7 cells in comparison to that in the controls. The colonies of HeLa, MCF7, and Huh7 cells exposed to germylene **3** were fewer in number and smaller in size in comparison to that in the respective controls. As the 25 $\mu$M solution of compound **3** showed the maximum reduction in the cell viability in the MTT assay, this concentration of compound **3** was used for performing all the trypan blue and colony formation assays. Taken together, all the aforementioned cell culture experiments illustrate the (a) dose-dependent cytotoxicity of compound **3** towards human cancer cell lines (HeLa, MCF7, and Huh7) and (b) existence of cell-type-specific differences in the antiproliferative effects of compound **3**.

To investigate the cytotoxicity of compound **3** on a normal epithelial cell line, we used Vero cells derived from the kidney of a healthy adult African green monkey. Cisplatin and doxorubicin were also tested on Vero cells along with compound **3** using MTT assay. As with cisplatin and doxorubicin, we found that the cytotoxicity of compound **3** on Vero cells was less pronounced in comparison to that in cancer cells [Figure 3(d)]. For examining if compound **3** has any anti-bacterial activity, we studied the growth

kinetics of Gram-positive [*Staphylococcus aureus (S.aureus*)] and Gram-negative [*Escherichia coli* (*E.coli*)] bacteria in the presence of compound **3** (Figure S26; see SI).

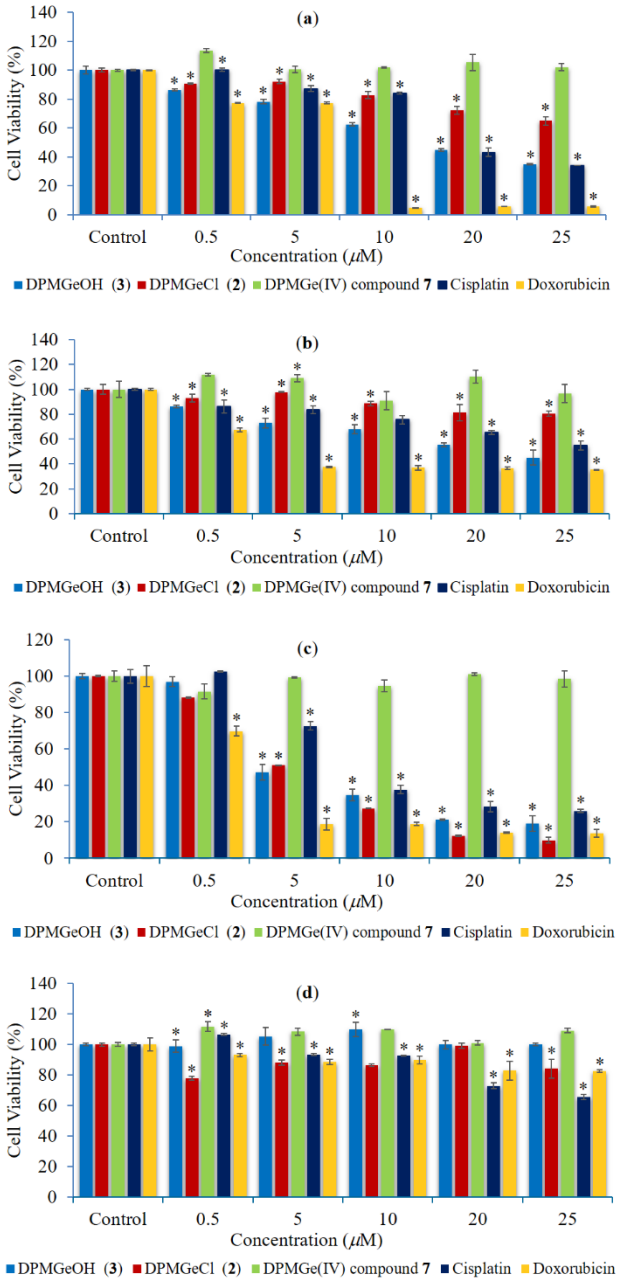



**Figure 3.** Suppression of cell proliferation by DPMGeOH (**3**), DPMGeCl (**2**), Ge(IV) compound **7**, cisplatin, and doxorubicin on HeLa (a), MCF7 (b), Huh7 (c), and Vero cells (d) as measured using MTT assay.*P-value <0.05. Control = cells treated with DMSO.

Interestingly, compound **3** did not show any antibacterial effect, unlike the chemotherapeutic agents cisplatin and doxorubicin which have documented antimicrobial activity.[14] Further, to ascertain that germylene **3** is not acting as a source of pro-ligand (DPMH) or a germanium(IV) species which is responsible for the observed cytotoxicity in human cancer cells, we performed additional experiments. The effect of pro-ligand (DPMH) on HeLa, MCF7, Huh7, and Vero cells was studied through MTT assay (Figure 5). We found that DPMH does not show cytotoxicity; this conclusion is corroborated by the Trypan blue (Figure S24) and colony formation assays (Figure 4 and Figure S25; see SI).

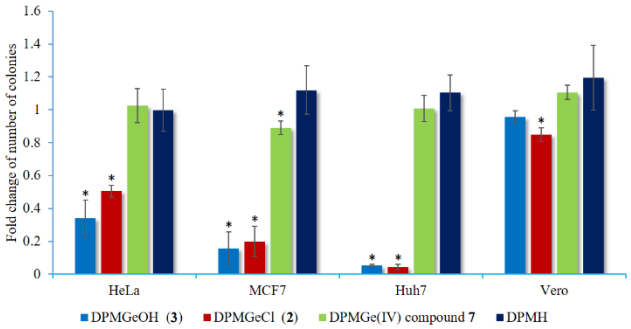



**Figure 4.** The colony formation assay carried out using 25 $\mu$M solution of DPMGeOH (**3**), DPMGeCl (**2**), Ge(IV) compound **7**, and DPMH (**1**) on HeLa, MCF, Huh7, and Vero cells. The respective solvent controls were normalized to one, and the increase/decrease of colonies is shown as fold change. *P-value <0.05. Control = cells treated with DMSO (for compounds **3**, **2**, and **7**) / THF (for compound **1**).

Furthermore, an isolable germanium(IV) compound, DPMGe(Cl)(Me)OTf (**7**), was studied for its biological activity. Compound **7** was synthesized through the reaction of compound **2** with MeOTf (Scheme S3; See SI).

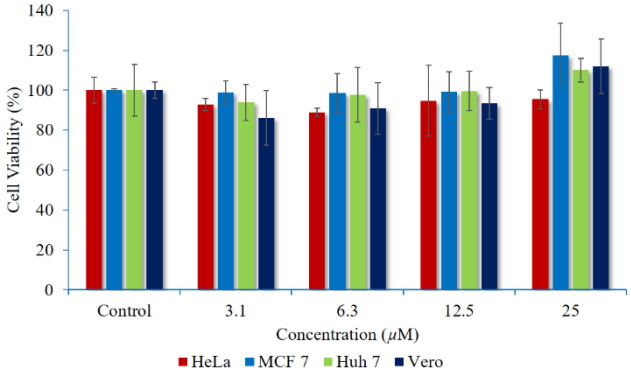



**Figure 5.** Effect of DPMH (**1**) on HeLa, MCF, Huh7, and Vero cells studied through MTT assay. Control = cells treated with THF. Owing to the evaporation tendency of THF, the assays were performed at a starting concentration of 25 $\mu$M and serial doubling dilutions were done up to 3.1 $\mu$M concentration.

Compound **7** was characterized by NMR spectroscopy (Figures S16-S18; see SI) and single-crystal X-ray diffraction studies (Figure S23; see SI). The effect of compound **7** on cell proliferation was analyzed through MTT assay on HeLa, MCF7, Huh7, and Vero cells (Figure 3). The results show that compound **7** does not possess antiproliferative properties. The findings from the Trypan blue and colony formation assays on HeLa, MCF7, Huh7, and Vero cells vindicate the outcomes of the MTT assay (Figure 4 and Figures S24-S25; see SI). Attempts were also made to isolate other germanium(IV) compounds, such as DPMGe(Cl)(Me)(I) and DPMGe(=O)OH, for evaluating their cytotoxicity. To synthesize DPMGe(Cl)(Me)(I), reactions of compound **2** were carried out with one equivalent as well as with an excess of MeI (Scheme S4; see SI). Both the reactions failed to produce the desired Ge(IV) compound DPMGe(Cl)(Me)(I). For the synthesis of DPMGe(=O)OH, a reaction of compound **3** with $N_2O$ was tried to find the occurrence of no reaction between them (Scheme S5; see SI). We also tested germylene **2** that is not

stable in the culture medium to the extent of compound **3** (vide infra), for its antiproliferative properties on HeLa, MCF7, Huh7, and Vero cells using MTT assay (Figure 3). The antiproliferative properties of compound **2** are comparable to that of compound **3** suggesting that germylene is responsible for the antiproliferative effect. The Trypan blue and colony formation assays on HeLa, MCF7, Huh7, and Vero cells substantiate this conclusion (Figure 4 and Figures S24-S25; see SI). We anticipate that the decomposition of compound **2** in the culture medium is most likely due to sodium bicarbonate in the culture medium (Figure S27; see SI). For this purpose, a reaction of compound **2** with sodium bicarbonate was carried out (Scheme 6; see SI); this experiment revealed that compound **2** completely gets converted to compound **3** (Figure S28; see SI). These findings confirm that germylene **3** is the species responsible for the antiproliferative properties against human cancer cells.

In summary, we have isolated a culture-medium stable germylene **3** and demonstrated its potential biological application. Its antiproliferative effects on human cancer cells MCF7 and Huh7 were marginally better than that of cisplatin, while on HeLa cells the effects are comparable. The cytotoxicity of germylene **3** on normal epithelial cells was comparable or marginally lower to that of the anti-cancer drugs cisplatin and doxorubicin. Our results highlight yet unknown applications of germylenes; this work lays the foundation for future studies on the biological properties of germylenes. The findings also shed light on how unstable main-group compounds can be made stable and used in the biological domain for essential applications.

**Keywords:** biogermylene chemistry • germylene • metallylene • anti-proliferation • bioorganometallic chemistry

[1] For examples, see, a) J. J. Wilson, S. J. Lippard, *Chem. Rev.*, **2014**, *114*, 4470−4495; b) D. Wang, S. J. Lippard, *Nature Reviews Drug Discovery,* **2005**, *4,* 307-320.

[2] For examples, see, a) A. L. Demain, P. Vaishnav, *Microbial Biotechnology*, **2011**, *4*, 687–699; b) G. M. Cragg, P. G. Grothaus, D. J. Newman, *Chem. Rev.*, **2009**, *109*, 3012–3043.

[3] For examples, see, a) L. Qi, Q. Luo, Y. Zhang, F. Jia, Y. Zhao, F. Wang, *Chem. Res. Toxicol.* **2019**, *32*, 1469−1486; b) T. Lazarevic, A. Rilak, Z. D. Bugarcic, *Eur. J. of Med. Chem.* **2017**, *142*, 8-31; c) P. Zhang, P. J. Sadler, *Eur. J. Inorg. Chem.* **2017**, 1541-1548; d) M. Cini, T. D. Bradshaw, S. Woodward, *Chem. Soc. Rev.* **2017**, *46*, 1040-1051; e) L. Zeng, P. Gupta, Y. Chen, E. Wang, L. Ji, H. Chao, Z.-S. Chen, *Chem. Soc. Rev.* **2017**, *46*, 5771-5804; f) S. K. Fung, T. Zou, B. Cao, P.Y. Lee, Y. M. E. Fung, D. Hu, C. N. Lok, C. M. Che, *Angew. Chem. Int. Ed.*, **2017**, *56*, 3892-3896; g) W. Liu, R. Gust, *Coord. Chem. Rev.* **2016**, *329*, 191-213; h) S. Medici, M. Peana, V. M. Nurchi, J. I. Lachowicz, G. Crisponi, M. A. Zoroddu, *Coord. Chem. Rev.,* **2015**, *284*, 329-350; i) G. Jaouen, A. Vessiéresab, S. Top, *Chem. Soc. Rev.*, **2015**, *44*, 8802-8817; j) F. Cisnetti, A. Gautier, *Angew. Chem. Int. Ed.,* **2013**, *52*, 11976-11978; k) N. P. E. Barry, P. J. Sadler, *ACS Nano,* **2013**, *7*, 5654-5659; l) U. Jungwirth, C. R. Kowol, B. K. Keppler, C. G. Hartinger, W. Berger, P. Heffeter, *Antioxid Redox Signal.*, **2011**, *15*, 1085–1127; m) M. Frezza, S. Hindo, D. Chen, A. Davenport, S. Schmitt, D. Tomco, Q. P. Dou, *Curr Pharm Des.*, **2010**, *16*, 1813–1825; n) C. G. Hartinger, P. J. Dyson, *Chem. Soc. Rev.*, **2009**, *38*, 391–401.

[4] For examples, see, a) A. Attanzio, M. Ippolito, M. A. Girasolo, F. Saiano, A. Rotondo, S. Rubino, L. Mondello, M. L. Capobianco, P. Sabatino, L. Tesoriere, G. Casella, *J. Inorg. Biochem.* **2018**, *188*, 102–112; b) L. Rocamora-Reverte, E. Carrasco-García, J. Ceballos-Torres, S. Prashar, G. N. Kaluđerovic´, J. A. Ferragut, S. Gómez-Ruiz, *ChemMedChem*, **2012**, *7*, 301-310; c) S. K. Hadjikakou, N. Hadjiliadis, *Coord. Chem. Rev.* **2009**, *253*, 235-249.

[5] For examples, see, a) P. Lu, S. Yao, J. Cai, P.-h. Yang, *Bioorg. Med. Chem. Lett.* **2014**, *24*, 5294-5297; b) L. G. Menchikov, M. A. Ignatenko, *Pharma. Chem. J.* **2013**, *46*, 635-638; c) G. Zhai, W. Zhu, Y. Duan, W. Qu, Z. Yan, *Main Group Met. Chem.* **2012**, *35*, 103-109.

[6] For examples, see, a) M. Asay, C. Jones, M. Driess, *Chem. Rev*. **2011**, *111*, 354-396; b) Y. Mizuhata, T. Sasamori , N. Tokitoh, *Chem. Rev*. **2009**, *109*, 3479-3511; c) A. V. Zabula, F. E. Hahn, *Eur. J. Inorg. Chem*. **2008**, 5165-5179; d) W.-P. Leung, K.-W. Kan, K.-H. Chong, *Coord. Chem. Rev*. **2007**, *251*, 2253-2265.

[7] For examples, see, a) C. Hering-Junghans, P. Andreiuk, M. J. Ferguson, R. McDonald, E. Rivard, *Angew. Chem. Int. Ed.* **2017**, *56*, 6272–6275; b) F. Walz, E. Moos, D. Garnier, R. Köppe, C. E. Anson, F. Breher, *Chem. Eur. J.* **2017**, *23*, 1173-1186; c) N. Del Rio, A. Baceiredo, N. Saffon-Merceron, D. Hashizume, D. Lutters, T. Müller, T. Kato, *Angew. Chem. Int. Ed.* **2016**, *55*, 4753-4758; d) S. Yao, Y. Xiong, T. Szilvási, H. Grützmacher, M. Driess, *Angew. Chem. Int. Ed*. **2016**, *55*, 4781-4785; e) M. Walewska, J. Baumgartner, C. Marschner, L. Albers, T. Müller, *Chem. Eur. J.* **2016**, *22*, 18512-18521; f) T. Ochiai, T. Szilvási, D. Franz, E. Irran, S. Inoue, *Angew. Chem. Int. Ed.* **2016**, *55*, 11619-11624; g) S. Sinhababu, D. Yadav, S. Karwasara, M. K. Sharma, G. Mukherjee, G. Rajaraman, S. Nagendran, *Angew. Chem. Int. Ed*. **2016**, *55*, 7742-7746; h) A. Rit, J. Campos, H. Niu, S. Aldridge, *Nat. Chem*. **2016**, *8*, 1022-1026; i) L. Álvarez-Rodríguez, J. A. Cabeza, P. García-Álvarez, D. Polo, *Coord. Chem. Rev*. **2015**, *300*, 1-28; j) K. Inomata, T. Watanabe, H. Tobita, *J. Am. Chem. Soc.* **2014**, *136*, 14341−14344; k) Y.-L. Shan, W.-L. Yim, C.-W. So, *Angew. Chem. Int. Ed.* **2014**, *53*, 13155-13158; l) B. Su, R. Ganguly, Y. Li, R. Kinjo, *Angew. Chem. Int. Ed*. **2014**, *53*, 13106-13109; m) L. Li, T. Fukawa, T. Matsuo, D. Hashizume, H. Fueno, H. Tanaka, K. Tamao, *Nat. Chem*. **2012**, *4*, 361-365.

[8] For examples, see, a) T. J. Hadlington, C. E. Kefalidis, L. Maron, C. Jones, *ACS Catal.* **2017**, *7*, 1853–1859; b) N. Del Rio, M. Lopez-Reyes, A. Baceiredo, N. Saffon-Merceron, D. Lutters, T. Müller, T. Kato, *Angew. Chem. Int. Ed*. **2017**, *56*, 1365-1370; c) J. Schneider, C. P. Sindlinger, S. M. Freitag, H. Schubert, L. Wesemann, *Angew. Chem. Int. Ed.* **2017**, *56*, 333-337; d) Y. Wu, C. Shan, Y. Sun, P. Chen, J. Ying, J. Zhu, L. Liu, Y. Zhao, *Chem. Commun.* **2016**, *52*, 13799-13802; e) T J. Handlington, M. Hermann, G. Frenking, C. Jones *J. Am. Chem. Soc.* **2014**, *136*, 3028-3031; f) R. K. Siwatch, S. Nagendran, *Chem. Eur. J.* **2014**, *20,* 13551-13556.

[9] For examples, see, a) M. Usher, A. V. Protchenko, A. Rit, J. Campos, E. L. Kolychev, R. Tirfoin, S. Aldridge, *Chem. Eur. J.* **2016**, *22*, 11685-11698; b) T. J. Hadlington, M. Hermann, G. Frenking, C. Jones, *Chem. Sci.* **2015**, *6*, 7249-7257; c) J. D. Erickson, P. Vasko, R. D. Riparetti, J. C. Fettinger, H. M. Tuononen, P. P. Power, *Organometallics* **2015**, *34*, 5785-5791; d) K. Inomata, T. Watanabe, Y. Miyazaki, H. Tobita, *J. Am. Chem. Soc.* **2015**, *137*, 11935−11937; e) S. K. Mandal, H. W. Roesky, *Acc. Chem. R.* **2012**, *45*, 298-307; f) X. Wang, Z. Zhu, Y. Peng, H. Lei, J. C. Fettinger, P. P. Power, *J. Am. Chem. Soc*. **2009**, *131*, 6912-6913;

[10] M. J. Polking, H. Zheng, R. Ramesh, A. P. Alivisatos, *J. Am. Chem. Soc*. **2011**, *133*, 2044-2047.

[11] C. K. Jha, S. Karwasara, S. Nagendran, *Chem. Eur. J*. **2014**, *20*, 10240-10244.

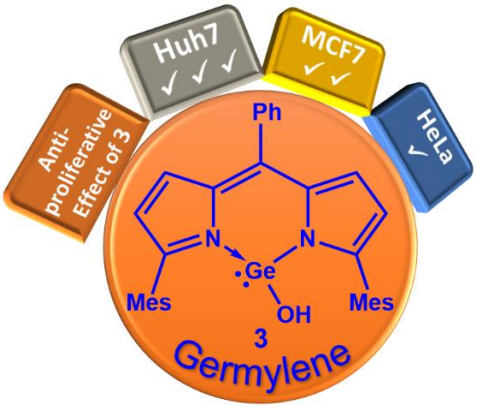
[12] a) L. W. Pineda, V. Jancik, H. W. Roesky, D. Neculai, A. M. Neculai, *Angew. Chem. Int. Ed.* **2004**, *43*, 1419-1421; b) W. Wang, S. Inoue, S. Yao, M. Driess, *Organometallics* **2011**, *30*, 6490-6494.

[13] L. Ferro, P. B. Hitchcock, M. P. Coles, J. R. Fulton, *Inorg. Chem*. **2012**, *51*, 1544-1551.

[14] a) K. Joyce, S. Saxena, A. Williams, C. Damurjian, N. Auricchio, S. Aluotto, H. Tynan, A. L. Demain, *The Journal of Antibiotics*, **2010**, *63*, 530; b) V. Peiris, B. A. Oppenheim, *J. Clin. Pathol.* **1993**, *46*, 1124-1125.

## Entry for the Table of Contents

**Biogermylene Chemistry:** The biological application of a germylene is demonstrated. It shows strong antiproliferative effects on cancer cell lines, but it is only minimally toxic to normal epithelial cells.

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**A Prelude to Biogermylene Chemistry**