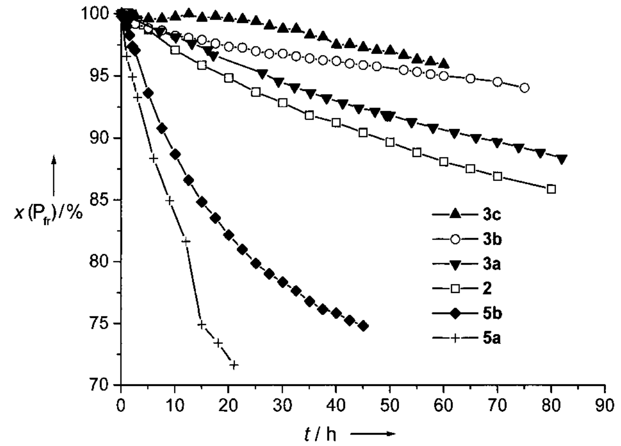

Figure 2. Kinetics of the thermal $P_{fr} \rightarrow P_r$ isomerization of the recombinant phyA65-**2**, -**3a**–**c**, and -**5a**,**b** phytochromes at ambient temperature. The P_{fr} samples were prepared by saturating irradiation of the corresponding P_r forms.

The steric interactions between ring D of the chromophore and the amino acids of the protein pocket significantly influence the rates of the chromophore binding to the apoprotein and the thermal reversal of P_{fr} to P_r. Relative to phytochromes with a native chromophore, which possess a C_1 substituent at C17 and a C_2 substituent at C18 (such as phyA65-**1** and -**3a**), the changes in reactivity depend on the position of the substituent(s) modified, C17 or C18, with C17 being more sensitive. Thus, the assembly of the 17-ethyl and 17-isopropyl homologues **5a** and **5b** is clearly slower than that of the respective C18 regioisomeric analogues **3a** and **3b**. The extreme blue shift of the P_r form of phyA65-**5b** (λ_{max} = 550 nm) may reflect a particularly strong steric constraint by the protein, which forces ring D of the chromophore out of plane with regard to rings A–C and thus interrupts conjugation of the π system.[5] A blue shift in absorption which is almost as large (λ_{max} = 576 nm) has also been observed for phyA124-**6**,[6] brought about upon interruption of conjugation due to the 15,16-saturated bridge between rings C–D of the phycoerythrobilin chromophore **6**. Whereas **6** cannot form a P_{fr} because of the saturated C15–C16 bond, we find for P_{fr} of **5b** only a moderately blue-shifted maximum (see Table 1). As another reason for the blue shift, a weakening of the protonation state, for example, by an increase of the distance between proton donor and chromophore, appears possible. In this context a decrease in absorption to accompany the blue shift would be expected upon deprotonation of the chromophore, as in the transition from the 17-ethyl (**5a**) to the 17-isopropyl isomer (**5b**).

Experimental Section

Synthesis of the linear tetrapyrroles **2**, **3b**, **c**, and **5a**, **b**:

The total syntheses of the new tetrapyrroles followed the convergent strategy of A-B+C-D → A-B-C-D previously described.[7] The various ring D substitution patterns were made accessible by adaptation of a previously developed pyrrole synthesis[8] based on addition of an aldehyde to a nitroalkane, acetylation, and coupling with *tert*-butyl isocyanoacetate.

The oxidation of 2,5-unsubstituted pyrroles to pyrrol-2-ones[9] was not regiospecific. Both regioisomers resulting from the unsymmetrically substituted pyrroles could be used separately after chromatographic separation for the synthesis of the two homologous series of tetrapyrroles.

While all the 4-methylpyrrol-2-ones coupled with the ring C component in good yields, the 4-isopropyl homologue was obtained in very low yield, probably due to steric crowding. Attempts to achieve coupling with the 4-*tert*-butyl derivative failed entirely.

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Isolated Hexagonal Channels Built up by Three-Connected Ge^- Ions in LiGe at High Pressure**

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In the homologous series of LiE compounds (E = Group 14 elements Si–Pb), LiSi[1, 2] and LiGe[3, 4] are Zintl phases at normal pressure (NP),[5, 6] but LiSn[7] and LiPb[8, 9] belong to the class of intermetallic phases. Owing to a charge transfer Li^+Si^- and Li^+Ge^-, the Si^- and the Ge^- ions in these Zintl phases are isovalence-electronic to the elements of Group 15, and build up the three-dimensional three-coordinate net of the MgGa-type structure[10] with three homonuclear bonds. However, in the intermetallic compounds LiSn[7] and LiPb,[8, 9]

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the Sn atoms have four and six homonuclear contacts, respectively. Therefore due to the change of bonding within these series of LiE compounds, LiGe and LiSn are ambivalent compounds and one can expect a shift in bonding if different temperatures and pressures are applied. Treatment of NP-LiGe at 4 GPa and 600 °C in a belt apparatus is sufficient to prepare a tetragonal LiGe high-pressure (HP) phase,[11] in which there are twice as many two-coordinate Ge^{2-} ions as four-coordinate Ge^0 atoms. The electron balance demands a total of $16\,e^-$ for two Ge^{2-} ions ($2 \times 6 = 12$ valence electrons e^-) and one Ge^0 atom ($4\,e^-$); however, in 3 LiGe there are only $15\,e^-$ available. The Zintl phase NP-LiGe is transformed into a "near-Zintl-phase"[12] The oppsosite effect is observed for NP-LiSn. Slowly cooling a LiSn melt leads to the thermodynamically stable intermetallic phase α-LiSn.[7] However, if a Li-Sn-Ga melt is cooled, β-LiSn[13] is obtained, which is isotypic with the tetragonal phase HP-LiGe and thus also a "near-Zintl-phase".

Surprisingly, it is also possible to prepare a second hexagonal HP LiGe phase in a belt apparatus at 4 GPa and 900 °C. This phase is also quenchable to ambient conditions. Crystallographic data for the three LiGe phases are presented in Table 1. Inspection of this table shows that there is only a small difference in density and in unit cell volume between the hexagonal and the tetragonal HP phases of LiGe. The increase in density in relation to the NP phase is 9.6 % for tetragonal HP-LiGe and 9.2 % for hexagonal HP-LiGe.

Table 1. Crystallographic data of the three LiGe phases.[3, 4, 11]

	LiGe(ND)	LiGe(HD)	LiGe(HD)
crystal system	tetragonal	tetragonal	hexagonal
space group	$I4_1/a$	$I4_1/amd$	$P6_3/mmc$
a [Å]	9.810(3)	4.0529(1)	8.451(3)
c [Å]	5.807(2)	23.282(3)	6.198(3)
V [Å^3]	558.8(4)	382.4(1)	383.4(4)
Z	16	12	12
ρ_{calcd} [g cm^{-3}]	3.782	4.145	4.135

Table 2. Number of neighbors, interatomic distances [Å],[a] and Ge-Ge-Ge angle [°].[3, 4, 11]

	LiGe(ND) tetragonal		LiGe(HD)[b] tetragonal		LiGe(HD) hexagonal	
Ge neighbors	3 Ge:	2.560 (2 ×), 2.655 (1 ×)	4 Ge_{II}: 2 Ge_I:	2.70 2.70	3 Ge:	2.55 (2 ×), 2.56 (1 ×)
	8 Li:	2.66, 2.73, 2.77, 2.82, 3.07, 3.11, 3.17, 3.54	8 Li (Ge_I):	2.87 (4 ×), 2.88 (4 ×)	8 Li:	2.71, 2.73 (2 ×), 2.80, 3.00, 3.02 (2 ×), 3.09
			8 Li (Ge_{II}):	2.70 (2 ×), 2.84 (2 ×), 2.88 (4 ×)		
Ge-Ge-Ge [°]	105, 109, 117		Ge_I:	97 (2 ×), 116 (4 ×)	102 (2 ×), 116	
			Ge_{II}:	97		
Li-Li [Å]	2.91, 2.97		2.66, 2.88		2.44, 2.71, 2.73, 3.00, 3.02, 3.09, 3.10	

[a] Standard deviation [Å]: NP-LiGe: Ge–Ge, Li–Ge: ± 0.005; Li–Li: ± 0.01; HP-LiGe tetragonal: Ge–Ge: ± 0.01, Li–Ge: ± 0.03, Li–Li: ± 0.05; HP-LiGe hexagonal: Ge–Ge: ± 0.01, Li–Ge: ± 0.05, Li–Li: ± 0.08. [b] Tetragonal HP-LiGe[11] contains four four-connected (Ge_I) and eight two-connected Ge atoms (Ge_{II}) as well as four Li atoms in the centers of the Ge eight-membered rings (Li_I) and eight Li atoms above or below the two-connected Ge atoms (Li_{II}).

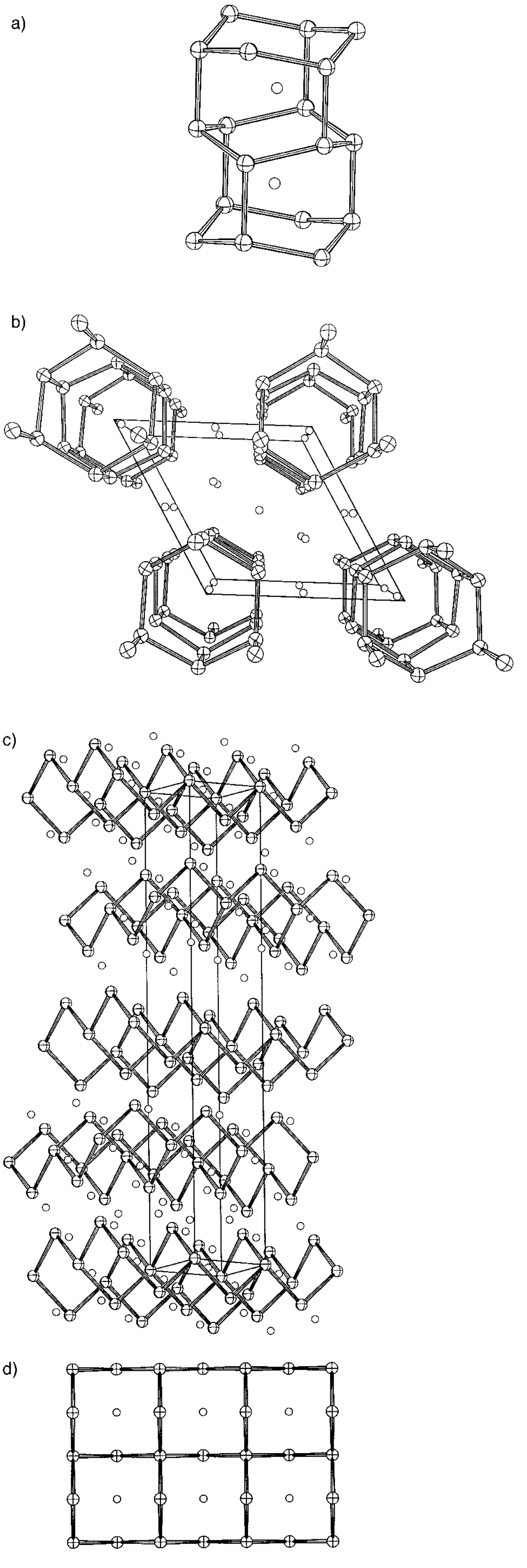
Table 2 gives the number of neighbors, interatomic distances, and Ge-Ge-Ge bond angles. In both the NP-LiGe and hexagonal HP-LiGe phases, Ge atoms form three homonuclear bonds.

Therefore both are Zintl phases consisting of Li^+ and Ge^- ions, in contrast to tetragonal HP-LiGe, which is, as already mentioned, only a "near Zintl phase" with twice as many two-coordinate as four-coordinate Ge atoms. The Ge^- ions in hexagonal HP-LiGe build up puckered six-membered rings of distorted chairs, which are stacked above each other (Figure 1 a). The Ge–Ge bonds in the chair are 2.55 Å long and form angles of 116° (Table 2). The third Ge–Ge bond (2.56 Å) connects the chair with adjacent chairs alternating up or down (Figure 1 a); the Ge-Ge-Ge angle is 102°. This leads to puckered six-membered rings of distorted boats; ideal chairs and boats have bond angles of 109.5°. Figure 1 b shows a perspective view along [001] (the stacking axis) of the hexagonal HP-LiGe phase which reveals a new motif: three-connected Ge^- ions build up hexagonal channels. These channels, centered at the corners of the unit cell, are 4.13 Å apart, a distance more than 1.6 times the Ge–Ge bond length. Such an arrangement of isolated hexagonal channels built up by three-coordinate ions is observed here for the first time for a Zintl phase. Li^+ counterions are found in the center of the hexagonal channels and in the symmetry-equivalent positions between them.

Figure 1 c, d shows clearly that tetragonal HP-LiGe[11] has a layer structure with a sequence of four layers each consisting of two- and four-coordinate germanium. One third of the Li^+ counterions are found in the center of the Ge eight-membered rings, one third lie above and one third lie below the two-coordinate Ge^{2-} ions. Figure 1 e depicts the three-dimensional net of three-coordinate Ge^- ions in NP-LiGe,[3, 4] in which puckered eight-membered germanium rings are arranged along fourfold screw axes. Six such puckered Ge eight-membered rings are shown which are connected by two fourfold counterrotating screw axes (4_3, 4_1). In each Ge eight-membered ring there are four Li^+ counterions in a distorted tetrahedral arrangement.

In all three LiGe phases each germanium atom has eight Li neighbors (Table 2), and each lithium atom has eight Ge neighbors (not shown in Table 2), leading to 8:8 coordination. Whereas in the NP-LiGe phase the Ge–Li distances range between 2.66 and 3.54 Å, in both HP phases this range is smaller (2.70 – 2.88 Å for the tetragonal and 2.71 – 3.09 Å for the hexagonal phase). Additionally, Table 2 shows that many of the Li–Li distances in the HP phases are shorter than those in the NP phase. The shortest Li–Li distance is 2.91 Å in the NP phase, 2.66 Å in the tetragonal HP phase, and 2.44 Å in the hexagonal HP phase.

In addition to the 8:8 coordination for the three LiGe phases, there is another common feature. All three phases



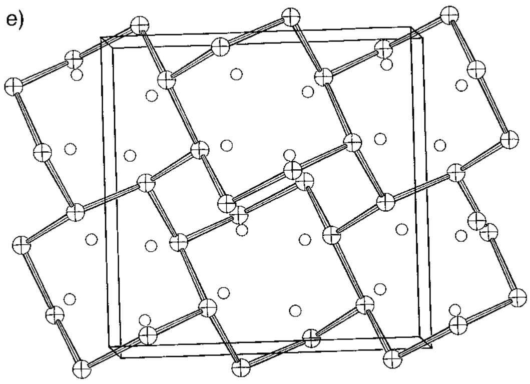


Figure 1. ORTEP plots for the three LiGe phases. a) View along a section of a hexagonal channel (large circles with a cross: Ge, small circles: Li) of hexagonal high-pressure phase. b) Perspective view along [001] of the hexagonal HP phase. c) Layer structure of the tetragonal HP phase.[11] Here only a section with six eight-membered rings comprising two- and four-coordinate Ge atoms per layer is shown; for reasons of clarity the Li^+ ions were omitted from the central layer. d) One Ge layer of the tetragonal HP phase (view along [001]); a Li^+ ion is located in the center of each eight-membered ring. e) The tetragonal NP phase (view along [001]).[3, 4] For details see text.

show a structural motif which is reminiscent of elemental germanium. Cubic germanium (3C-Ge) consists of four-connected atoms that build puckered six-membered rings of ideal chairs, which are stacked in the [111] direction with a repeat unit of three layers. Puckered eight-membered rings of four-connected atoms are stacked along the cubic axes. Both tetragonal phases NP-LiGe and HP-LiGe contain puckered eight-membered rings, in contrast hexagonal HP-LiGe has puckered six-membered rings. In NP-LiGe these eight-membered rings are connected to form a three-dimensional net along [001] (Figure 1 e), whereas in the tetragonal HP-LiGe phase they are arranged parallel (001) and build up a layer structure (Figure 1 c, d). In the hexagonal HP-LiGe phase the puckered six-membered rings lie directly above each other, in elemental 3C-Ge they are shifted towards each other leading to a repeat unit of three layers (Figure 1 b). Analogous to hexagonal wurtzite as well as diamond with a sequence of two layers, hexagonal germanium (2H-Ge, $a = 3.94(5)$, $c = 6.55(5)$ Å)[14] consists of six-membered rings of chairs that lie directly above each other. This arrangement also leads to boats as in HP-LiGe. Compared to 2H-Ge, in hexagonal HP-LiGe the a axis is doubled and additionally increased by 6%, whereas the c axis is slightly decreased by 5% (Table 1). Therefore, hexagonal HP-LiGe can be derived simply from 2H-Ge by doubling the a axis, then removing the four Ge atoms connecting the germanium chairs within the same layer, and finally filling the Li ions into the channels and into the symmetry-equivalent positions between them!

Experimental Section

NP-LiGe, which was prepared by melting Li and Ge in a water-cooled copper boat under argon, was converted into the HP phase in a belt apparatus in boron nitride and molybdenum crucibles at typically $p = 4$ GPa, $T = 900\,^{\circ}C$. After 20 min, the heating was stopped and the pressure was released 5 min later. Heating the new phase at 1 bar to 300 °C led in an exothermic reaction quantitatively to the thermodynamically stable NP phase. X-ray photographs of a crystal of the new HP phase ($Cu_{K\alpha}$ radiation) showed Laue symmetry 6/*mmm* (systematic absences: *hhl* with $l = 2n$) and the lattice parameters $a = 8.45$, $c = 6.20$ Å. However, the quality of the crystal was not sufficient to perform a structure determination on a four-circle diffractometer. Therefore structural parameters were determined on powder material with a Guinier diffractometer. The approximate Ge and Li positions were derived from Patterson and Fourier syntheses.[15] Refinement was performed by the Rietveld method.[16–18] Hexagonal HP-LiGe was obtained as a phase mixture with 20% germanium (calculated from the scaling factors [19] of the Rietveld refinement). Owing to the extreme conditions in the preparation, the mobile Li^+ ions show high thermal parameters.[18]

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A New Phase-Switch Method for Application in Organic Synthesis Programs Employing Immobilization through Metal-Chelated Tagging**

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The increasing demand for large numbers of new compounds for biological testing has encouraged synthetic chemists to look for new technologies and strategies to produce these compounds in a fast, clean, and efficient way. Presently, the most popular way in which this can be achieved is by the use of solid-phase organic synthesis (SPOS). This methodology allows the use of an excess of reagents and at the end of the synthetic sequence the immobilized product is isolated following a simple filtration.[1] Unfortunately, there are considerable limitations to this approach: The reactions are often slower than their solution-phase counterparts, it is difficult to monitor the reaction progress, and long optimization times are often required to transfer solution-phase chemistry onto the polymer support. Owing to these limitations, new strategies combining the benefits of established protocols for solution-phase chemistry with the key advantages of solid-phase chemistry are being developed which allow multistep syntheses to be performed using an array of supported reagents and scavenging agents.[2] One particular feature of combinatorial chemistry programs is the challenge of product purification by using methods which can be automated and operated in a multiparallel mode.[3]

Herein we report a new strategy for the synthesis of small-molecule libraries based on the "catch and release" principle.[4] In this approach we have devised a method of *selectively and reversibly* immobilizing key intermediates within a conventional solution-phase-mediated reaction sequence. We argued that a phase switch/separation[2] could be effected by a reversible and selective noncovalent interaction between a resin-bound metal and an organic metal-chelating "tag" linked to the molecule of interest (Scheme 1).[5] Thus, the immobilization or "phase switching"[2] of the tagged intermediate upon completion of the solution-phase reaction would be realized by the addition of a resin-bound metal to

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