activities,[16] separation of membrane proteins by 2D electrophoresis,[17] creation of addressable arrays of modified lipid bilayer membranes for combinatorial chemistry,[18] and controlled cell culture on designed membrane surfaces.[19]

Experimental Section

Materials: Diacetylene lipid **1** and egg PC were purchased from Avanti Polar Lipids, Alabaster, AL, USA. NBD-PE (*N*-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)-1,2-dihexadecanoyl-*sn*-glycero-3-phosphoethanolamine) was purchased from Molecular Probes, Eugene, OR, USA.

Lithographic polymerization of bilayers: Bilayers of **1** were deposited onto glass substrates from the air/water interface by the Langmuir–Blodgett (LB) and Langmuir–Schaefer (LS) methods (surface pressure $\pi = 35\ mN\,m^{-1}$). Prior to the photopolymerization, oxygen was removed from the aqueous solution by an argon gas purge. After the patterned polymerization, monomeric **1** was removed by immersing the sample in ethanol and subsequently rinsing it extensively with Milli-Q water. The fluorescence microscope observation has been made using excitation and observation wavelength of 490 nm and 530 nm, respectively.

Incorporation of new lipid bilayers: Vesicle suspensions of egg PC/NBD-PE (1 mM in a 0.05 M phosphate buffer with 0.1 M NaCl (pH 7.0)) were extruded through a filter with pores of diameter ~50 nm. A small volume of filtered suspension (100 to 200 μL) was placed onto the patterned **1** bilayer samples and sandwiched with another slide glass with a thin cover glass in between in order to avoid scratching the patterned surfaces. The sample was rinsed with the same buffer solution after 5 minutes.

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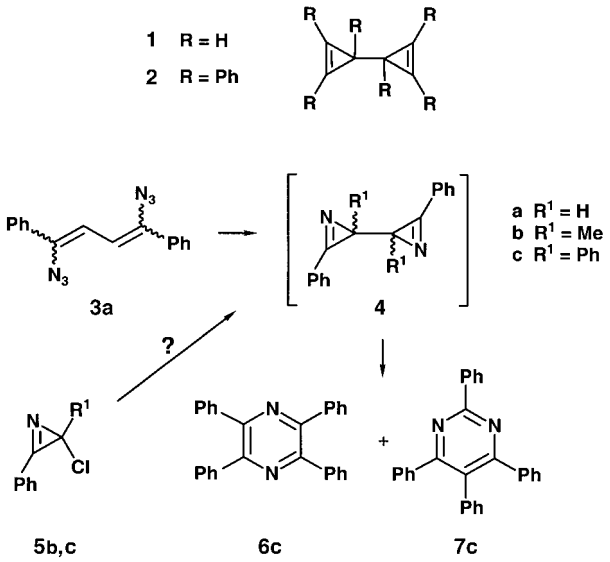
Synthesis of 1,4-Diazidobuta-1,3-dienes by Electrocyclic Ring Opening: Precursors for Bi-2*H*-azirin-2-yls and Their Valence Isomerization to Diazabenzenes**

Klaus Banert* and Frank Köhler

Dedicated to Professor Horst Kunz on the occasion of his 60th birthday

Bicycloprop-2-enyl **1** was isolated first in 1989 as the last remaining valence isomer of benzene (Scheme 1).[1] This compound, which was calculated to be the highest in energy of the $(CH)_6$ species,[2] polymerizes above $-10\,^{\circ}C$,[1] while other bicycloprop-2-enyls, for example **2**,[3] undergo a valence isomerization to give benzene derivatives on heating. Several



Scheme 1. Previous unsuccessful attempts to identify the bi-2*H*-azirin-2-yls **4**.

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mechanisms were proposed to explain these aromatization reactions.[4] Up to now, all attempts to prepare the heterocyclic analogues **4** failed, neither the double Neber reaction nor the coupling reaction of **5b** generated these bi-2*H*-azirin-2-yls.[5a] Later, Storr et al.[6] reported the treatment of **5c** with lithium, which was said to lead to **6c** (10% yield) and **7c** (10%) but not to tetraphenylpyridazine (**10c**). The postulated intermediate **4c** could not be observed. Attempts to generate **4a** from the diazide **3a** failed immediately because the starting material **3a** could not be prepared.[5] To the best of our knowledge, 1,4-diazidobuta-1,3-dienes are unknown.

Nevertheless, we consider the access via azides to be the most promising approach to investigate the highly strained heterocycles of type **4** and their valence isomerization. We describe here the synthesis of the diazides **3c–f** as well as the transformation into the biazirinyls **4c**,**d**,**f** and their aromatization.

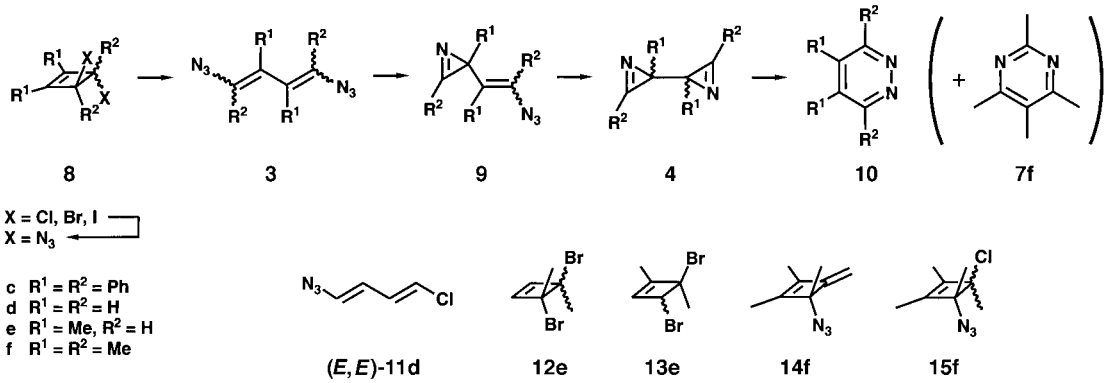
Results in the literature[5, 7] but also of our own efforts indicated quickly that classical methods[8] to prepare vinyl azides are unsuited for the synthesis of the diazides **3**. Thus, we generated these compounds by conrotatory ring opening of the cyclobutenes **8** (X = N_3; Scheme 2). Treatment of the dibromide *trans*-**8d**[9] (X = Br) or the analogous diiodide[9] with a concentrated (ca. 2 mol L^{-1}) solution of tributylhexadecylphosphonium azide (QN_3)[10] in chloroform (20 h or 80 min/20 °C, respectively) gave in addition to small amounts of the diazide *cis*-**8d** (7% or 6%, respectively) only the diazide (*E*,*E*)-**3d** (89% or 62%, respectively).[11, 12] Whereas isolated *cis*-**8d** (X = N_3) could not subsequently be converted into **3d**, the course of the ring opening of *trans*-**8d** (X = N_3) was so rapid that this intermediate was not detected by NMR spectroscopic monitoring of the reaction. However, the monosubstituted products, 3-azido-4-bromocyclobut-1-ene and the analogous iodo compound, could be detected as intermediates. Evidently, the azido groups accelerate the electrocyclic ring opening as effectively as other donor substituents such as alkoxy groups.[13] The compound **3d** could not be prepared with the aid of alternative reagents, for example, NaN_3/DMSO, or starting with less-reactive dihalides. On treatment with QN_3 at 50 °C the dichloride *cis*-**8d** gave rise to a mixture of other products, while a small amount of **10d** (10%) and the diene (*E*,*E*)-**11d** (62%) were formed on the reaction of *trans*-**8d**[9] (X = Cl) and QN_3 at 20 °C. However, a mixture[14] of the dibromide **8e** and the allyl isomers **12e** and **13e** afforded the open-chain product (*E*,*E*)-**3e** (34–37%) in addition to *cis*-**8e** (X = N_3, yield ca. 16%) on treatment with either NaN_3 or LiN_3 in DMSO or with QN_3/$CHCl_3$.

At first, we obtained only (*E*)-**9d** (up to 59%) or (*E*)-**9e** (up to 37%) by photolysis of (*E*,*E*)-**3d** or (*E*,*E*)-**3e**, respectively (CD_2Cl_2, −85 °C, high-pressure mercury lamp). Small amounts of the very unstable compound **4d** (8% yield, 3:2 mixture of diastereomers, Table 1) could only be detected when (*E*,*E*)-**3d** was irradiated in the presence of the sensitizing agent 9,10-dicyanoanthracene ($CDCl_3$, −50 °C). On warming the mixture of products from photolysis, **4d** degraded to furnish at best only traces of **10d**. Just like compound **1**, **4d** does not tend to aromatization.

To synthesize more stable diazides and biazirinyls, we treated *trans*-**8f**[15] (X = Cl) with QN_3 ($CHCl_3$, 20 °C) to give a mixture of diazides *trans*-**8f** (55%) and *cis*-**8f** (9%) as well as the monoazides **14f** (17%) and **15f** (2%+3%). After separation by chromatography, *trans*-**8f** (X = N_3) could be isolated because the electrocyclic ring opening to give (*E*,*E*)-**3f** is strongly decelerated by the inward rotation of the methyl groups. The target compound (*E*,*E*)-**3f** was generated only on warming in benzene (80 °C), whereby the secondary products (*E*)-**9f** and **10f**[16] are also formed. Prolonged heating led exclusively to **10f** (88%). On incomplete thermolysis of *trans*-**8f** (X = N_3), (*E*,*E*)-**3f** could be isolated in 14% yield based on converted diazide (*trans*-**8f**).

The *E* configuration of (*E*)-**9e**,**f** was determined from two-dimensional ^{1}H NMR nuclear Overhauser spectroscopy (2D-NOESY) experiments and nuclear Overhauser enhancement (NOE) difference spectra. Thus the configuration of (*E*,*E*)-**3e**,**f** is also confirmed. The *trans* structure of *trans*-**8f** (X = N_3) was established by the signals of the ^{1}H NMR spectra which exhibited very small low-field shifts in the presence of [Eu(fod)$_3$] (tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)europium(III)). The analogous spectra of the compounds *cis*-**8d–f** (X = N_3) showed changes of the chemical shifts at least 300 times greater since these diazides are able to interact with the shift reagent in a chelate-forming[17] manner.

On thermolysis, (*E*,*E*)-**3f** was transformed via (*E*)-**9f** into **10f** with high yield (97%). However, the photochemical reaction of (*E*,*E*)-**3f** (glass equipment, $CDCl_3$, −60 °C), which proceeded also via (*E*)-**9f** (with a proportion of up to 61%),



Scheme 2. Synthesis and valence isomerization of the bi-2*H*-azirin-2-yls **4**.

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Table 1. Selected physical data of compounds **3d–f**, **4c**,**d**,**f**, *trans*-**8f** (X = N_3), and **9c–f**.[a]

(*E*,*E*)-**3d**: Yellow solid, decomposition at room temperature; IR ($CDCl_3$): $\tilde{\nu}$ = 2111 cm^{-1} (N_3), 1253 (N_3); UV/Vis (acetonitrile): λ_{max}(lg ε) = 296 nm (4.52); ^{1}H NMR ($CDCl_3$): δ = 5.87 (AA′XX′, 2H), 6.12 (AA′XX′, 2H), from simulation: $^3J(AX) = {}^3J(A'X') = 13.3$ Hz, $^3J(AA') = 11.5$ Hz, $^5J(XX') = 1.0$ Hz, $^4J(AX') = {}^4J(A'X) = -0.5$ Hz; ^{13}C NMR ($CDCl_3$): δ = 116.39 (d), 127.97 (d)

(*E*,*E*)-**3e**: Yellow solid, m.p. 48 °C (hexane, decomp); IR ($CDCl_3$): $\tilde{\nu}$ = 2100 cm^{-1} (N_3), 1258 (N_3); UV/Vis (cyclohexane): λ_{max}(lg ε) = 300 nm (4.46); ^{1}H NMR ($CDCl_3$): δ = 1.75 (d, ^4J = 1.1 Hz, 6H; Me), 6.26 (q, ^4J = 1.1 Hz, 2H; 1-H/4-H); ^{13}C NMR ($CDCl_3$): δ = 11.97 (q; Me), 123.14 (d; C-1/C-4), 125.13 (s; C-2/C-3)

(*E*,*E*)-**3f**: Yellow oil; IR ($CDCl_3$): $\tilde{\nu}$ = 2108 cm^{-1} (N_3), 1287 (N_3); UV/Vis (acetonitrile): λ_{max}(lg ε) = 255 nm (4.08); ^{1}H NMR ($CDCl_3$): δ = 1.66 (q, ^5J = 1.5 Hz, 6H), 1.86 (q, ^5J = 1.5 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 14.31 (q), 15.78 (q), 123.00 (s), 126.33 (s)

4c (Major (MI) and minor isomer (mi)): ^{1}H NMR ($CDCl_3$): δ = 6.80–7.80 (m); ^{13}C NMR ($CDCl_3$): δ = 45.49 (s; C-2, MI), 45.55 (s; C-2, mi), 122.73 (s; *i*-Ph, mi), 123.14 (s; *i*-Ph, MI), 126.40 (d; *p*-Ph, mi), 126.69 (d), 126.80 (d), 127.25 (d; *o*,*m*-Ph, MI), 127.93 (d), 128.10 (d; *o*,*m*-Ph, MI), 128.80 (d), 129.12 (d; *o*,*m*-Ph, MI), 129.61 (d), 129.63 (d; *o*,*m*-Ph, MI), 132.87 (d; *p*-Ph, mi), 132.97 (d), 139.77 (s; *i*-Ph, mi), 140.70 (s; *i*-Ph, MI), 163.72 (s; C-3, MI), 163.98 (s; C-3, mi)

4d (Major isomer): ^{1}H NMR (−50 °C, $CDCl_3$): δ = 1.68 (s, 2H; 2-H), 10.09 (s, 2H; 3-H); ^{13}C NMR (−50 °C, $CDCl_3$): δ = 28.32 (d; C-2), 165.75 (d; C-3)

4d (Minor isomer): ^{1}H NMR (−50 °C, $CDCl_3$): δ = 1.98 (s, 2H; 2-H), 9.91 (s, 2H; 3-H); ^{13}C NMR (−50 °C, $CDCl_3$): δ = 28.70 (d; C-2), 166.89 (d; C-3)

4f (More stable isomer): IR ($CDCl_3$): $\tilde{\nu}$ = 1753 cm^{-1} (C=N); ^{1}H NMR (−50 °C, $CDCl_3$): δ = 1.00 (s, 6H; 2-Me), 2.44 (s, 6H; 3-Me); ^{13}C NMR (−50 °C, $CDCl_3$): δ = 14.53 (q), 19.78 (q), 38.95 (s; C-2), 176.25 (s; C-3)

4f (Less stable isomer): ^{1}H NMR (−50 °C, $CDCl_3$): δ = 1.16 (s, 6H; 2-Me), 2.38 (s, 6H; 3-Me); ^{13}C NMR (−50 °C, $CDCl_3$): δ = 14.71 (q), 20.25 (q), 38.92 (s; C-2), 173.75 (s; C-3)

trans-**8f** (X = N_3): Colorless oil; IR ($CDCl_3$): $\tilde{\nu}$ = 2093 cm^{-1} (N_3), 1251 (N_3); UV/Vis (acetonitrile): λ_{max}(lg ε) = 208 nm (3.74); ^{1}H NMR ($CDCl_3$): δ = 1.42 (s, 6H), 1.64 (s, 6H); ^{13}C NMR ($CDCl_3$): δ = 8.69 (q; Me), 17.86 (q; Me), 72.67 (s; C-3/C-4), 141.28 (s; C-1/C-2)

9c: IR ($CDCl_3$): $\tilde{\nu}$ = 2110 cm^{-1} (N_3), 1738 (C=N), 1255 (N_3); ^{1}H NMR ($CDCl_3$): δ = 6.88–7.63 (m, 20H); ^{13}C NMR ($CDCl_3$): δ = 44.78 (s; C-2), 123.50 (s), 126.11 (d), 126.37 (d), 127.24 (d), 127.68 (d), 127.75 (d), 128.25 (d), 128.40 (d), 128.53 (d), 128.95 (d), 129.09 (d), 129.75 (d), 131.86 (d), 133.26 (s), 137.63 (s), 139.04 (s), 142.19 (s), 165.51 (s; C-3), one signal (s) not resolved

(*E*)-**9d**: ^{1}H NMR (−80 °C, CD_2Cl_2): δ = 2.33 (dd, ^3J = 8.9 Hz, ^3J = 2.0 Hz, 1H; 2-H), 4.77 (ddd, $^3J_{trans}$ = 13.5 Hz, ^3J = 8.9 Hz, ^4J = 0.6 Hz, 1H; 1′-H), 6.38 (d, $^3J_{trans}$ = 13.5 Hz, 1H; 2′-H), 10.06 (dd, ^3J = 2.0 Hz, ^4J = 0.6 Hz, 1H; 3-H); ^{13}C NMR (−80 °C, CD_2Cl_2): δ = 26.16 (d; C-2), 119.54 (d), 127.89 (d), 164.80 (d; C-3)

(*E*)-**9e**: ^{1}H NMR (−85 °C, CD_2Cl_2): δ = 1.14 (d, ^4J = 1.3 Hz, 3H; 1′-Me), 1.31 (d, ^4J = 1.5 Hz, 3H; 2-Me), 6.20 (qd, ^4J = 1.3 Hz, ^5J = 0.8 Hz, 1H; 2′-H), 10.26 (qd, ^4J = 1.5 Hz, ^5J = 0.8 Hz, 1H; 3-H); ^{13}C NMR (−85 °C, CD_2Cl_2): δ = 13.65 (q; Me), 20.73 (q; Me), 33.65 (s; C-2), 122.48 (d; C-2′), 128.31 (s; C-1′), 172.53 (d; C-3)

(*E*)-**9f**: ^{1}H NMR ($CDCl_3$): δ = 1.28 (s, 3H; 2-Me), 1.63 (q, ^5J = 1.5 Hz, 3H; 1′-Me), 2.12 (q, ^5J = 1.5 Hz, 3H; 3′-H), 2.44 (s, 3H; 3-Me); ^{13}C NMR ($CDCl_3$): δ = 12.58 (q), 13.40 (q), 14.39 (q), 22.39 (q), 36.13 (s; C-2), 124.75 (s), 127.61 (s), 174.49 (s; C-3)

[a] ^{1}H NMR: 300 MHz; ^{13}C NMR: 75 MHz, assignments of signals by distortionless enhancement by polaritation transfer (DEPT) experiments.

led quantitatively to a 1:1 mixture of *meso*-**4f** and *rac*-**4f**. On warming the irradiated solution, both stereoisomers were converted into **10f** in quantitative first-order reactions. One of these valence isomerizations occurred already with $k = 3.65 \cdot 10^{-4}\,s^{-1}$ at −25 °C, the other with $k = 1.73 \cdot 10^{-4}\,s^{-1}$ at +10 °C. So far, we could not clarify which compound has the *meso* structure and which the *rac* configuration. We suppose that the new N–N bond is formed in the rate-determining step of the aromatization. For conformational reasons, this should be more difficult for *meso*-**4f** which may thus be the kinetically more stable stereoisomer. In the presence of $AgBF_4$, the more stable isomer of **4f** was completely transformed into **7f**[18] at −25 °C, whereas the other stereoisomer again gave **10f**. Photolysis of (*E*,*E*)-**3f** in the more UV transparent CD_3CN (quartz equipment, −40 °C) furnished (*E*)-**9f** and **4f** first and then, after prolonged irradiation, a mixture of **7f** (30%) and **10f** (22%) as well as the fragmentation products but-2-yne (3–4%) and acetonitrile (3–4%).[19] By using these conditions, prolonged photolyses of the diazides *cis*-**8f** or *trans*-**8f** proceeded via **4f** and resulted in the formation of both aromatics **7f** (13% or 12%, respectively) and **10f** (33% or 41%, respectively) as well as traces of but-2-yne and acetonitrile.

We monitored the reaction of **8c**[20] (X = Br) with QN_3 in $CDCl_3$ by NMR spectroscopy at low temperature. Even at −25 °C nucleophilic substitution and electrocyclic ring opening proceeded so rapidly that only the signals of **3c** could be assigned with certainty. At +5 °C, a slow evolution of nitrogen started,[21] in the course of which one isomer of **9c** and after that both stereoisomers of **4c** (ca. 2:1) could be detected unequivocally (Table 1). Only the aromatic compound **10c**[22] (87% based on dibromide **8c**) was found after prolonged reaction times or after slight warming of the reaction mixture whereas the heterocycles **6c** and **7c** could not be identified. Thus, the postulated[6] generation of **4c** from **5c** seems to be questionable.

The 1,4-diazidobuta-1,3-dienes **3d–f** presented here could be used as synthetic building blocks for cycloaddition reactions, as shown by some examples in Scheme 3. At present, we are trying to synthesize biazirinyls **4** which bear sterically more demanding groups R^1 and exhibit a higher thermal stability. Valence isomerizations of **4** with $R^1 \neq R^2$ may enable plausible conclusions regarding the reaction mechanism to be drawn.

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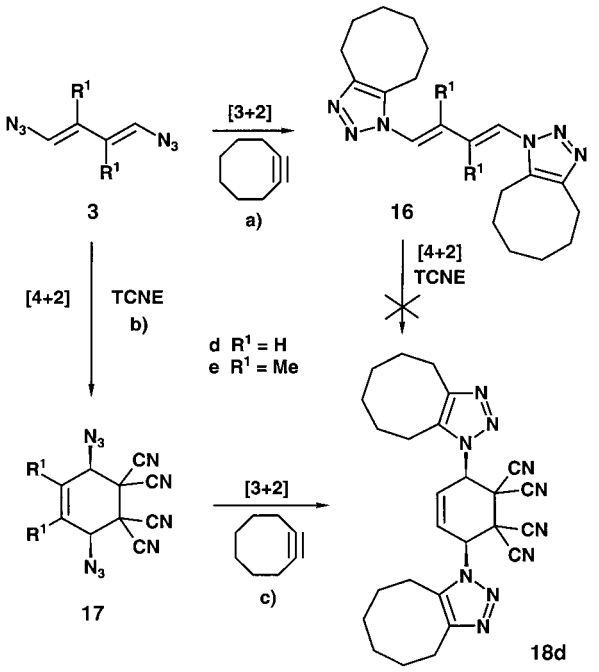

Scheme 3. Cycloaddition reactions of 1,4-diazidobuta-1,3-dienes **3d**,**e**. a) Chloroform, 20 °C, 30 – 60 min, 86 % **16d**, 99 % **16e**; b) acetone, tetracyanoethylene (TCNE) 20 °C, 2 – 20 h, 95 % **17d**, 91 % **17e**; c) chloroform, 20 °C, 3 h, 96 % **18d**.

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[11] Caution should be exercised during isolation of azides, particularly (*E*,*E*)-**3d** which is explosive.

[12] Isolated yield; the yield of unstable products, which could not be isolated, e.g. **4** and **9**, was determined by ^{1}H NMR spectroscopy (internal standard).

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Highly Enantioselective Isomerization of 4,7-Dihydro-1,3-dioxepins Catalyzed by Me-DuPHOS-Modified Dihalogenonickel Complexes and Determination of the Absolute Configuration of the Isomerization Products**

Herbert Frauenrath,* Dirk Brethauer, Stefan Reim, Martin Maurer, and Gerhard Raabe

Dihalogenonickel complexes bearing chiral ligands have proved to be efficient catalyst precursors for the asymmetric isomerization of cyclic allyl acetals. In the isomerization of 5-methylen-1,3-dioxanes to 5-methyl-4*H*-1,3-dioxins, for example, DIOP-modified (DIOP = 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphanyl)butane) dihalogenonickel complexes activated with lithium triethylborohydride gave selectivities of up to 92 % *ee*.[1] The enantioselectivities significantly decreased, when 4,7-dihydro-1,3-dioxepins (**1**) were used as substrates. However, we have shown previously that the selectivities depend on the relationship between the chelate-ring size of the catalyst and the ring size of the substrate.[1, 2] Thus, isomerization of **1a** by using a five-membered CHIRAPHOS-modified (CHIRAPHOS = 2,3-bis(diphenylphosphanyl)butane) dichloronickel complex (**2a**) at room temperature in THF afforded 2-*tert*-butyl-4,5-dihydro-1,3-dioxepin (**3a**) with 67 % *ee*. In contrast, the seven-membered DIOP-modified dichloronickel complex gave **3a** under the same reaction conditions with only 38 % *ee*.[3]

Searching for other diphosphanes that form five-membered-ring nickel chelates we found that 1,2-bis(phospholanyl)benzenes (Me-DuPHOS, Et-DuPHOS) are suitable ligands for the asymmetric nickel-catalyzed isomerization of **1**.[4, 5] In fact, by employing Me-DuPHOS as a ligand a breakthrough was achieved in terms of enantioselectivity (Table 1). Treatment of **1a** with [$NiCl_2$((−)-Me-DuPHOS)] (**2c**) at room temperature and activation with $LiBHEt_3$ in toluene provided (−)-**3a** already with 85 % *ee* (Table 1, entry 5), but incomplete conversion at this temperature indicated a decreased catalytic activity of the dichloronickel complex (**2c**). However, we found that replacing the chloro by bromo or iodo ligands drastically enhanced the activity of the nickel catalysts. Thus, isomerizations of **1** with CHIRAPHOS and DuPHOS bearing $NiBr_2$– or NiI_2 – phosphane complexes could be performed even at low temperatures yielding vinyl

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[+] X-ray crystallographic analysis

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