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Synthesis of indoles and tryptophan derivatives *via* photoinduced nitrene C–H insertion†

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Functionalized indoles and tryptophans can be obtained from stannylated alkenes and *o*-iodoanilines *via* Stille coupling. Subsequent azidation and photochemical nitrene generation results in the formation of the heterocyclic ring systems *via* C–H insertion.

Introduction

Indoles belong to the most important and interesting heterocycles, not only because of their widespread distribution in nature, but also from a pharmaceutical point of view.[1] The indole ring system is found in relatively simple compounds such as the neurotransmitter serotonin, but also in the rather complex indole alkaloids, such as the lysergic acid derivatives (Fig. 1).[2] In general, these compounds are formed biosynthetically from tryptophan, possibly in combination with enzymatic modifications (hydroxylation, halogenation, prenylation).[3] Functionalized tryptophans are also widespread in biologically active peptides,[4] such as the chondramides[5] or the cyclocinamides.[6] With respect to that, it is not surprising that a wide range of synthetic protocols have been developed for the synthesis of the indole nucleus.[7]

In principle, one can differentiate between two major approaches. The first one starts with an existing indole ring system, which is modified by substitution. The other one generates the indole nucleus, whereby in most cases the five membered heterocyclic ring is formed. According to this approach, most syntheses start with *o*-substituted nitrobenzenes or aniline derivatives. Besides the classical indole syntheses a wide range of transition metal catalysed methods have been developed during the last decades.[8] Some of them, such as the Larock protocol[9] are based on the coupling of *o*-iodoanilines with alkynes,[10] or start directly with *o*-allylated[11] or *o*-alkynylated anilines.[12] These approaches give access to 2- or 2,3-substituted indoles and are especially suitable for the synthesis of highly substituted indoles. However, they are unsuitable for the synthesis of tryptophans and derivatives thereof, where the 2-position is unsubstituted. This problem can be solved by using silyl-substituted alkynes, followed by protodesilylation.[13]

For the synthesis of tryptophans, Pd-catalysed annulation of *o*-haloanilines with δ-oxo amino acids can be used (Scheme 1a),[14] or the cyclization of amino acid derived nitrostyrenes (Scheme 1b).[15] The stereogenic α-centre can be introduced by auxiliary control.[13] Alternatively, the stereochemical outcome can be controlled by reacting chiral auxiliaries with the corresponding 3-substituted indoles,[16] or by asymmetric hydrogenation of β-unsaturated amino acid derivatives.[17] Recent approaches are based on asymmetric cross coupling reactions such as Negishi couplings,[18] or on stereoselective

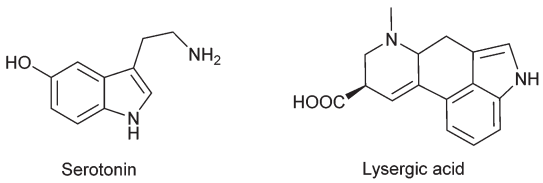
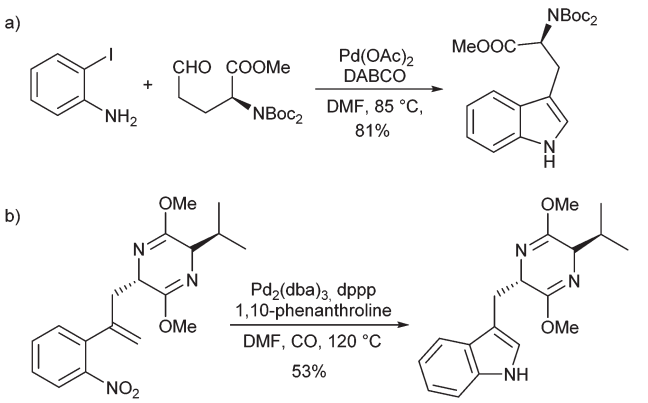


Fig. 1 Naturally occurring indole derivatives.



Scheme 1 Selected examples of transition metal-catalysed tryptophane syntheses.

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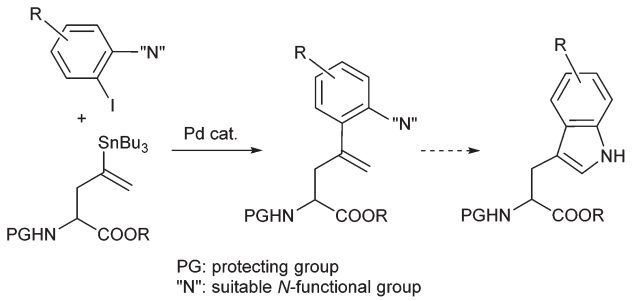
additions of azlactones onto vinyl indoles in the presence of chiral Brønsted acids.[19] Regioselective C–H activations allow the subsequent functionalization at the 2-, 4- and 6-position.[20]

Our group has been involved in the synthesis of unusual amino acids[21] since a couple of years. As a synthetic tool we use chelated glycine ester enolates,[22] which can be subjected to a wide range of reactions, such as aldol reactions,[23] Michael additions[24] or transition metal catalysed allylic alkylations.[25] Stannylated allylic acetates and carbonates provide access to metallated amino acids that can be subjected to further modifications *via* Stille couplings.[26] Since these cross couplings proceed under completely neutral conditions, no epimerization of stereogenic centres occurs, and therefore, this protocol is suitable for natural product and drug synthesis.[27] Herein, we describe a new synthetic route toward substituted indoles and tryptophans, based on cross couplings of stannylated intermediates and subsequent photochemical nitrene C–H insertion (Scheme 2).

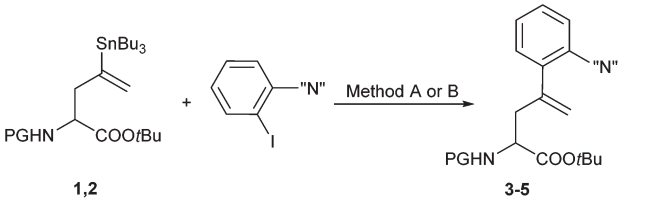
Results and discussion

In our previous investigations, in general, we obtained the best results with TFA-protected *tert*-butyl glycinate as nucleophile, especially in Pd-catalysed allylic alkylations. Therefore, we started our investigations with stannylated allyl glycine derivative **1** (Table 1).[28] To gain direct access to the desired azido-substituted styrene derivative, we subjected **1** to a Stille coupling with *o*-azidoiodobenzene, evaluating several catalysts and reaction conditions. In all cases, complex product mixtures were obtained, resulting, for example, from a decomposition of the azide. In addition, the formation of allyl glycine was observed as a result of protodestannation of **1**.[29] By far the best results were obtained employing a protocol from Baldwin *et al.*,[30] which uses an excess of CsF and catalytic amounts of CuI and $Pd(PPh_3)_4$. Under these mild conditions, the expected coupling product **3a** could be obtained in almost 50% yield (Table 1, entry 1). A slightly better result was obtained in the coupling of *o*-iodoaniline (entry 2). The moderate yield in this case was also caused by protodestannation of **1**. We assumed that under the reaction conditions CsF acts as a base, removing the proton from the rather acidic trifluoroacetamide. The HF formed might be the reason for the protodestannation



Scheme 2 Tryptophan synthesis *via* Stille coupling/C–H insertion.

Table 1 Optimization of the reaction conditions for Stille couplings



1,2 3-5

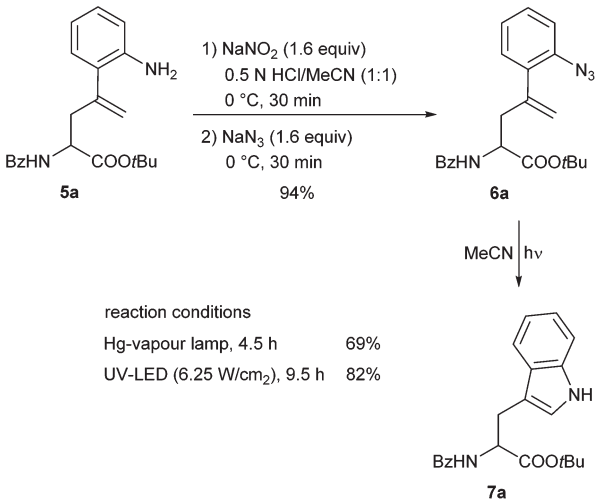
Entry	Stannane	PG	"N"	Method	Product	Yield [%]
1	**1**	TFA	N_3	A	**3a**	49
2	**1**	TFA	NH_2	A	**4a**	61
3	**2**	Bz	NH_2	A	**5a**	91
4	**1**	TFA	NH_2	B	**4a**	90

Method A: $Pd(PPh_3)_4$ (5 mol%), CuI (10 mol%), CsF (2.0 equiv.), DMF, 45 °C; Method B: $Pd(PPh_3)_4$ (5 mol%), CuI (2.0 equiv.), LiCl (2.0 equiv.), DMF, 80 °C, 18 h.

reaction. Therefore, we replaced the TFA protecting group by the less acidic benzoyl group (entry 3), and indeed, the yield of the desired coupling product **5a** could be increased to 91%. In this case, the formation of *N*-benzoylated allylglycine was not observed. Since obviously CsF caused the problems in case of **1**, we tried to find reaction conditions avoiding such basic additives. For the coupling of sterically demanding vinylstannanes, Corey *et al.* developed a protocol abstaining CsF completely, while using 6 equiv. of LiCl and 5 equiv. of CuI in DMSO.[31] This method requires higher reaction temperatures, but proceeds under completely neutral conditions. In our case, the best results were obtained with 2 equiv. of LiCl and CuI each in DMF. Under these conditions, the TFA-derivative **1** could also be coupled in excellent yield (entry 4). Attempts to use this protocol also for the direct coupling of iodo phenylazide were not successful, the yield under these conditions was even lower (26%) than in the preciously used method.

Since the azido group obviously is not the best functionality for Stille couplings, we next focused on its generation and direct nitrene formation/C–H insertion. Amines can easily be converted into azides *via* diazotization and subsequent reaction of the diazonium salt with azide. Use of *tert*-butylnitrite and $TMSN_3$ [32] provided the desired azide **6a** in 74% yield. But even better results could be obtained with $NaNO_2/NaN_3$ [33] in a 1 : 1 mixture of 0.5 N HCl and MeCN (to increase solubility of the components) (Scheme 3).

An elegant protocol to convert aryl azides into the corresponding nitrenes is their treatment with transition metal complexes, *e.g.*, of Rh[34] or Ru.[35] This approach is well suited for the synthesis of 2-substituted indoles, but fails in the case of 2-unsubstituted indoles. Treatment of **6a** with $Rh_2(OAc)_4$ provided only traces of the desired tryptophan **7a**. However, upon standing during storage in the laboratory, we observed that **6a** was cumulatively contaminated with **7a**. Obviously, visible light was able to "decompose" the azide. Therefore, we subjected **6a** to irradiation with a mercury vapour lamp, giving rise to the desired tryptophan **7a** in good yield (Scheme 3).[36]



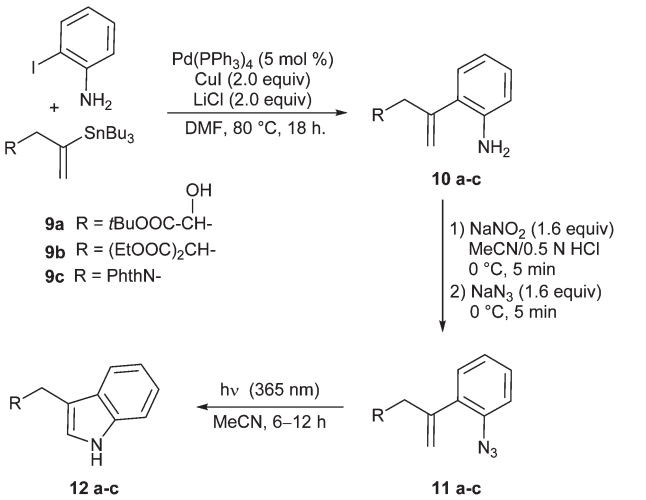
Scheme 3 Photochemical tryptophan synthesis.

To suppress photochemical side reactions by the high-energy irradiation we next investigated irradiation at 365 nm, using an adjustable UV-LED lamp. Indeed, under these conditions the yield could be further increased to 82%.

The optimized reaction conditions found application in the synthesis of various protected and substituted tryptophan derivatives (Table 2). Both Stille coupling protocols provided comparably good results and also the diazotization/azide formation delivered good to excellent yields. The yields of the photochemical C–H insertions were generally in the range of 65–80%. Only the methoxy-substituted derivatives were found to be less effective (entries 3 and 4). The application of *o*-iodonaphthylamine allows the synthesis of benzotryptophans (entry 8).

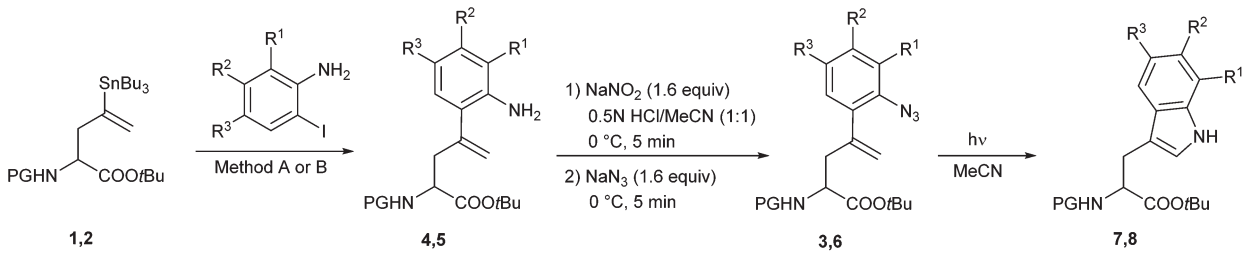
Although this procedure was especially developed for the synthesis of tryptophans, it is of course not limited to this substance class. *Via* allylic alkylation also a series of other functionalized vinyl stannanes can be obtained, such as the corresponding α-hydroxy esters,[37] malonates or protected amines.[26b] They could all be converted into the corresponding indole derivatives with comparable success (Table 3).

Table 3 Synthesis of functionalized indoles **10–12**



	Yields					
Stannane	**10**	[%]	**11**	[%]	**12**	[%]
9a	**10a**	69	**11a**	60	**12a**	75
9b	**10b**	83	**11b**	89	**12b**	86
9c	**10c**	69	**11c**	69	**12c**	77

Table 2 Synthesis of substituted tryptophans



Entry	Stannane	PG	Method	R^1	R^2	R^3	Aniline	Yield [%]	Azide	Yield [%]	Tryptophan	Yield [%]
1	**2**	Bz	A	H	H	Me	**5b**	70	**6b**	95	**7b**	78
2	**2**	Bz	A	H	H	Cl	**5c**	72	**6c**	89	**7c**	66
3	**2**	Bz	A	H	H	OMe	**5d**	77	**6d**	84	**7d**	56
4	**2**	Bz	A	H	OMe	H	**5e**	71	**6e**	71[a]	**7e**	34
5	**2**	Bz	A	H	H	COOEt	**5f**	59	**6f**	87	**7f**	67
6	**1**	TFA	B	H	H	H	**4a**	89	**3a**	87	**8a**	75
7	**1**	TFA	B	H	H	Me	**4b**	74	**3b**	92	**8b**	81
8	**1**	TFA	B	–CH=CH–CH=CH–		H	**4g**	66	**3g**	91	**8g**	71

Method A: $Pd(PPh_3)_4$ (5 mol%), CuI (10 mol%), CsF (2.0 equiv.), DMF, 45 °C, 18 h.; Method B: $Pd(PPh_3)_4$ (5 mol%), CuI (2.0 equiv.), LiCl (2.0 equiv.), DMF, 80 °C, 18 h. [a] (1) $NaNO_2$ (1.6 equiv.), 15 s; (2) NaN_3 (1.6 equiv.), 30 min.

Conclusions

In conclusion, we could show that Stille couplings of stannylated amino acids with iodoanilines generate *o*-amino styrenes, which can easily be converted into the corresponding azides. Photochemical C–H insertion of an *in situ* generated nitrene generates indoles and tryptophans in a highly efficient manner. Applications of this protocol to the stereoselective synthesis of tryptophan-containing peptides are currently under investigation.

Experimental

General experimental details

All air- or moisture-sensitive reactions were carried out in dried glassware (>100 °C) under an atmosphere of argon. THF was distilled over Na/benzophenone prior to use. Dichloromethane (DCM), MeCN and DMF (anhydrous) were purchased from Sigma-Aldrich. EtOAc and petroleum ether (PE) were distilled prior to use. Reactions were monitored by analytical TLC, which was performed on silica gel on TLC PET-foils by Sigma-Aldrich. Visualization was accomplished with UV-light (254 nm), $KMnO_4$ solution or an iodine chamber. Rotary evaporation was conducted at 40 °C. The products were purified by flash chromatography on silica gel columns (Macherey-Nagel 60, 0.063–0.2 mm) or by automated flash chromatography (Grace Reveleris®, Teledyne Isco RediSep R_f silica cartridges). Mixtures of EtOAc and hexanes were generally used as eluents. Melting points were determined with a melting point apparatus IA 9100 by Electrothermal and are uncorrected. ^{1}H, ^{13}C and ^{119}Sn spectra were recorded with a Bruker AV II 400 [400 MHz (^{1}H), 100 MHz (^{13}C), 149 MHz (^{119}Sn)] spectrometer in $CDCl_3$ (+0.01% $Si(CH_3)_4$) unless otherwise specified. NMR spectra were evaluated using iNMR (Version 5.4.4). Chemical shifts are reported in ppm relative to $Si(CH_3)_4$ and $CHCl_3$ was used as the internal standard [$\delta(^1H)$ = 7.26 ppm, $\delta(^{13}C)$ = 77.0 ppm]. High resolution mass spectra were recorded with a Finnigan MAT 95 spectrometer using the CI technique. Photochemical experiments were conducted with a UV-LED [UV-LED SMART by Opsytec Dr Gröbel GmbH (max. irradiance >25 W cm^{-2}, λ = 365 nm, beam profile: standard, distance from reaction mixture: *ca.* 5 cm)].

***tert*-Butyl 2-benzoylamino-4-tributylstannyl-pent-4-enoate (2).** In a 250 mL Schlenk flask HMDS (5.90 mL 4.52 g, 28.0 mmol) was dissolved in THF (20 mL) and a 1.6 M *n*-BuLi solution (in hexanes) (15.6 mL, 25.0 mmol) was added dropwise at −78 °C. The solution was stirred for 10 min at room temperature and then cooled again to −78 °C. In another 100 mL Schlenk flask $ZnCl_2$ (1.64 g, 12.0 mmol) was carefully dried in vacuum (<0.1 mbar) with a heat gun. *tert*-Butyl hippurate (2.35 g, 10.0 mmol) was added and the flask was evacuated and refilled with Ar three times. THF (20 mL) was added, the solution was cooled to −78 °C and transferred to the cold LHMDS solution *via* cannula. The resulting yellow solution was stirred for 30 min at −78 °C to ensure complete transmetalation. A Schlenk tube was charged with [(allylPdCl)$_2$] (37 mg, 0.10 mmol) and PPh_3 (105 mg, 0.40 mmol), before THF (2 mL) was added and the solution was stirred for 10 min at room temperature. 2-(Tributylstannyl)allyl ethyl carbonate (3.35 g, 7.27 mmol) was added and the solution was added dropwise to the Zn-enolate solution at −78 °C. The reaction mixture was slowly warmed to room temperature overnight and stirred for 18 h. Subsequently, it was diluted with EtOAc (20 mL) before 1 M $KHSO_4$ solution (3 mL) was added. The layers were separated and the aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (hexanes/EtOAc/NEt_3 95 : 5 : 1), giving rise to **2** (3.69 g, 6.54 mmol, 90%) as a colorless viscous oil. R_f (**2**): 0.26 (hexanes/EtOAc 90 : 10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, J = 7.3 Hz, 9 H), 0.94 (m, 6 H), 1.28 (m, 6 H), 1.42–1.56 (m, 15 H), 2.60 (dd, J = 14.0, 9.1 Hz, 1 H), 2.92 (dd, J = 14.0, 4.9 Hz, 1 H), 4.58 (m, 1 H), 5.27 (dd, J_{Sn} = 59.6 Hz, J = 2.5 Hz, 1 H), 5.81 (dd, J_{Sn} = 128.5 Hz, J = 2.5 Hz, 1 H), 6.39 (d, J = 7.0 Hz, 1 H), 7.42 (m, 2 H), 7.49 (m, 1 H), 7.77 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.7 (d, $^1J_{Sn}$ = 333.3 Hz), 13.6, 27.3 (d, $^2J_{Sn}$ = 57.9), 28.1, 29.0 (d, $^3J_{Sn}$ = 19.8 Hz), 44.0, 52.9, 82.0, 127.0, 128.5, 128.7, 131.5, 134.1, 150.6, 166.8, 171.4 ppm. ^{119}Sn NMR (149.2 MHz, $CDCl_3$): δ = −43.0 ppm. HRMS (CI) *m*/*z* calcd for $C_{28}H_{47}NO_3Sn$ $[M]^+$: 565.2572. Found: 565.2577.

General procedures for Stille couplings

Method A. A dried Schlenk tube was charged with the organotin compound and the (substituted) *o*-iodoaniline in DMF (2 mL mmol^{-1}). CsF (2.0 eq.), CuI (10 mol%) and $Pd(PPh_3)_4$ were added and the mixture was stirred at 45 °C. After reaching full conversion (TLC) EtOAc and H_2O were added. Upon vigorous shaking (in the Schlenk tube) a colorless precipitate formed and the mixture was filtered through a pad of Celite® with EtOAc. The filtrate was dried over Na_2SO_4 and concentrated. The residue was purified by (automated) flash chromatography.

Method B. An oven dried Schlenk tube was charged with LiCl (2.0 eq.) and heated with a heat gun under vacuum (<0.1 mbar). After cooling to r.t. CuI (2.0 eq.), (substituted) *o*-iodoaniline (1.0 eq.) and $Pd(PPh_3)_4$ (5 mol%) were added and the flask was evacuated and refilled with Ar three times. DMF (10 mL mmol^{-1}), which was previously degassed by bubbling with Ar, and the organotin compound (1.2 eq.) was added and the mixture was heated to 80 °C for 18 h. After reaching full conversion (TLC) the mixture was diluted with EtOAc and 5 mL of 1 M KF-solution were added. Upon vigorous shaking (in the Schlenk tube) a colorless precipitate formed and the mixture was filtered through a pad of Celite® with EtOAc. The layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by (automated) flash chromatography.

***tert*-Butyl 4-(2-aminophenyl)-2-(2,2,2-trifluoroacetamido) pent-4-enoate (4a).** According to method B, 2-iodoaniline (55.9 mg, 0.250 mmol) was reacted with **1**[26] (172 mg,

0.300 mmol), LiCl (21 mg, 0.500 mmol), CuI (95 mg, 0.500 mmol) and $Pd(PPh_3)_4$ (14 mg, 12.5 μmol). Automated flash chromatography (hexanes/EtOAc 100 : 0 to 80 : 20) afforded **4a** (80 mg, 0.223 mmol, 89%) of **4a** as a colorless resin. R_f (**4a**): 0.37 (hexanes/EtOAc 80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 9 H), 2.95 (ddd, J = 14.1, 5.3, 1.4 Hz, 1 H), 3.08 (ddd, J = 14.3, 5.3, 1.0 Hz, 1 H), 3.83 (bs, 2 H), 4.58 (m, 1 H), 5.22 (d, J = 1.8 Hz, 1 H), 5.34 (m, 1 H), 6.70 (dd, J = 8.0, 0.9 Hz, 1 H), 6.75 (ddd, J = 7.5, 7.5, 1.1 Hz, 1 H), 6.96 (dd, J = 7.6, 1.4 Hz, 1 H), 7.07 (m, 1 H), 7.43 (d, J = 7.4 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.9, 38.7, 52.6, 83.2, 115.5 (q, J_F = 296.4 Hz), 116.3, 119.0, 119.6, 127.3, 128.5, 128.6, 142.2, 142.5, 146.4 (q, J_F = 37.5 Hz), 168.9 ppm. HRMS (CI) m/z calcd for $C_{17}H_{21}F_3N_2O_3$ $[M]^+$: 358.1499. Found: 358.1504.

***tert*-Butyl 4-(2-aminophenyl)-2-benzoylamino-pent-4-enoate (5a).** According to method A, 2-iodoaniline (418 mg, 1.91 mmol) was reacted with **2** (1.08 g, 1.91 mmol), CsF (580 mg, 3.82 mmol), CuI (36 mg, 0.191 mmol) and $Pd(PPh_3)_4$ (44 mg, 38 μmol). The reaction was worked up after 2 h. Automated flash chromatography (hexanes/EtOAc 100 : 0 to 70 : 30) afforded **5a** (628 mg, 1.66 mmol, 87%) as a brown solid, m.p. 87–88 °C. R_f (**5a**): 0.27 (hexanes/EtOAc 70 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (s, 9 H), 2.95 (dd, J = 14.0, 5.4 Hz, 1 H), 3.16 (ddd, J = 14.0, 5.1, 1.0 Hz, 1 H), 3.88 (bs, 2 H), 4.84 (ddd, J = 7.5, 5.2, 5.2, Hz, 1 H), 5.23 (d, J = 1.9 Hz, 1 H), 5.38 (m, 1 H), 6.64 (dd, J = 8.0, 1.1 Hz, 1 H), 6.72 (ddd, J = 7.5, 7.5, 1.1 Hz, 1 H), 6.77 (d, J = 7.5 Hz, 1 H), 6.99–7.04 (m, 2 H), 7.32 (m, 2 H), 7.41–7.48 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.1, 39.5, 52.9, 82.3, 116.0, 118.6, 119.2, 126.9, 127.7, 128.2, 128.3, 128.7, 131.3, 133.9, 142.7, 143.0, 166.6, 170.8 ppm. HRMS (CI) m/z calcd for $C_{22}H_{26}N_2O_3$ $[M]^+$: 366.1938. Found: 366.1938.

***tert*-Butyl 4-(2-aminophenyl)-2-hydroxypent-4-enoate (10a).** According to method B 2-iodoaniline (32.4 mg, 0.148 mmol) was reacted with **15**[36] (82 mg, 0.178 mmol), LiCl (13 mg, 0.296 mmol), CuI (56.4 mg, 0.296 mmol) and $Pd(PPh_3)_4$ (9 mg, 7.4 μmol). Automated flash chromatography (hexanes/EtOAc 100 : 0 to 80 : 20) yielded **10a** (27 mg, 0.103 mmol, 69%) as a colorless oil. R_f (**10a**): 0.26 (hexanes/EtOAc 70 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 9 H), 2.64 (ddd, J = 14.3, 8.5, 0.8 Hz, 1 H), 2.88 (m, 1 H), 3.10 (d, J = 5.8 Hz, 1 H), 3.92 (bs, 2 H), 4.08 (m, 1 H), 5.21 (m, 1 H), 5.39 (m, 1 H), 6.70 (dd, J = 8.0, 0.9 Hz, 1 H), 6.74 (m, 1 H), 7.02 (dd, J = 7.6, 1.5 Hz, 1 H), 7.07 (ddd, J = 7.9, 7.3, 1.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0, 42.6, 69.1, 82.6, 110.0, 115.8, 118.3, 118.4, 127.7, 128.2, 128.7, 142.8, 143.5, 173.8 ppm. HRMS (CI) m/z calcd for $C_{15}H_{21}NO_3$ $[M]^+$: 263.1516. Found: 263.1510.

Diethyl 2-[2-(2-aminophenyl)allyl]malonate (10b). According to method B 2-iodoaniline (130 mg, 0.582 mmol) was reacted with **16**[26b] (348 mg, 0.711 mmol), LiCl (50 mg, 1.19 mmol), CuI (227 mg, 1.19 mmol) and $Pd(PPh_3)_4$ (31 mg, 27 μmol). Automated flash chromatography (hexanes/EtOAc 100 : 0, 80 : 20) afforded **10b** (117 mg, 0.402 mmol, 69%) as an orange oil. R_f (**10b**): 0.23 (hexanes/EtOAc 80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 6 H), 2.98 (m, 2 H), 3.52 (t, J = 7.7 Hz, 1 H), 3.86 (bs, 2 H), 4.17 (q, J = 7.1 Hz, 4 H), 5.14 (m, 1 H), 5.29 (m, 1 H), 6.68 (m, 1 H), 6.71 (ddd, J = 7.2, 7.2, 1.2 Hz, 1 H), 6.98 (dd, J = 7.5, 1.6 Hz, 1 H), 7.07 (ddd, J = 9.0, 7.5, 1.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 35.6, 50.5, 61.5, 115.5, 116.6, 118.0, 126.8, 128.4, 128.8, 143.6, 144.0, 169.0 ppm. HRMS (CI) m/z calcd for $C_{16}H_{22}NO_4$ $[M + H]^+$: 292.1543. Found: 292.1581.

2-[2-(2-Aminophenyl)allyl]isoindoline-1,3-dione (10c). According to method B 2-iodoaniline (26 mg, 0.119 mmol) was reacted with **17**[26b] (68 mg, 0.143 mmol), LiCl (10 mg, 0.238 mmol), CuI (45 mg, 0.238 mmol) and $Pd(PPh_3)_4$ (6.9 mg, 6 μmol). Flash chromatography (hexanes/EtOAc 80 : 20) yielded **10c** (23 mg, 82.6 μmol, 69%) as a brown solid, m.p. 94–95 °C. R_f (**10c**): 0.29 (hexanes/EtOAc 70 : 30).^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.13 (bs, 2 H), 4.52 (m, 2 H), 5.18 (m, 2 H), 6.68–6.74 (m, 2 H), 7.07–7.12 (m, 2 H), 7.74 (m, 2 H), 7.88 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.4, 114.6, 115.3, 117.8, 123.4, 124.8, 128.9, 129.3, 132.0, 134.1, 142.0, 144.0, 168.1 ppm. HRMS (CI) m/z calcd for $C_{17}H_{14}N_2O_2$ $[M]^+$: 278.1050. Found: 278.1080.

General procedure for the diazotation/azidation of anilines[33]

The aniline derivative was dissolved in a mixture of MeCN and 0.5 M HCl (1 : 1, 0.05 M). Subsequently, $NaNO_2$ (1.6 equiv.) was added at 0 °C. After stirring for 5 min NaN_3 (1.6 equiv.) was added. After stirring for another 5 min, saturated $NaHCO_3$ solution was added and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo* and the residue was purified by (automated) flash chromatography.

***tert*-Butyl 4-(2-azidophenyl)-2-(2,2,2-trifluoroacetamido) pent-4-enoate (3a).** According to the general procedure for diazotation/azidation **4a** (74 mg, 0.206 mmol) was reacted with $NaNO_2$ (23 mg, 0.330 mmol) and NaN_3 (22 mg, 0.330 mmol). Flash chromatography (hexanes/EtOAc 90 : 10) afforded azide **3a** (69 mg, 0.179 mmol, 87%) as a colorless solid, m. p. 55–56 °C. R_f (**3a**): 0.53 (hexanes/EtOAC 80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 9 H), 2.94 (ddd, J = 14.5, 6.2, 0.6 Hz, 1 H), 3.27 (ddd, J = 14.5, 5.2, 0.8 Hz, 1 H), 4.47 (m, 1 H), 5.15 (d, J = 1.5 Hz, 1 H), 5.26 (m, 1 H), 6.79 (d, J = 6.8 Hz, 1 H), 7.09–7.16 (m, 3 H), 7.34 (ddd, J = 8.1, 6.8, 2.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.8, 38.1, 52.2, 83.2, 115.6 (d, J_F = 292.5 Hz), 118.4, 120.6, 125.0, 129.3, 130.5, 132.9, 137.1, 141.8, 156.3 (d, J_F = 37.4 Hz), 169.0 ppm. HRMS (CI) m/z calcd for $C_{17}H_{19}F_3N_2O_3$ $[M - N_2]^+$: 356.1342. Found: 356.1336.

***tert*-Butyl 4-(2-azidophenyl)-2-benzoylamino-pent-4-enoate (6a).** According to the general procedure for diazotation/azidation **5a** (113 mg, 0.270 mmol) was reacted with $NaNO_2$ (33 mg, 0.475 mmol) and NaN_3 (31 mg, 0.475 mmol). Automated flash chromatography (hexanes/EtOAc 100 : 0, 80 : 20) afforded azide **6a** (107 mg, 0.256 mmol, 95%) as a yellow resin. R_f (**6a**): 0.21 (hexanes/EtOAc 80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H), 2.98 (ddd, J = 14.4, 6.2, 0.8 Hz, 1 H), 3.31 (ddd, J = 14.4, 5.3, 1.0, Hz, 1 H), 4.71 (ddd, J = 7.6, 6.2, 5.3 Hz, 1 H), 5.12 (d, J = 1.7 Hz, 1 H), 5.29 (m, 1 H), 6.52 (d, J = 7.6 Hz, 1 H), 7.05 (dd, J = 8.0, 1.2 Hz, 1 H), 7.09 (ddd, J = 7.5, 7.5, 1.2 Hz, 1 H), 7.20 (dd, J = 7.5, 1.6 Hz, 1 H), 7.27 (ddd, J = 8.0, 7.6, 1.6 Hz,

1 H), 7.37 (m, 2 H), 7.47 (m, 1 H), 7.57 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0, 38.9, 52.3, 82.2, 118.4, 120.0, 124.9, 126.8, 128.4, 128.9, 130.6, 131.4, 133.7, 134.0, 137.1, 142.9, 166.4, 170.8 ppm. HRMS (CI) *m*/*z* calcd for $C_{22}H_{26}N_4O_3$ $[M + 2H]^+$: 394.1999. Found: 394.2002.

***tert*-Butyl 4-(2-azidophenyl)-2-hydroxypent-4-enoate (11a).** According to the general procedure for diazotation/azidation **10a** (26 mg, 98.7 μmol) was reacted with $NaNO_2$ (11 mg, 0.158 mmol) and NaN_3 (10 mg, 0.158 mmol). Flash chromatography (hexanes/EtOAc 80 : 20) afforded azide **11a** (17 mg, 58.8 μmol, 60%) as a colorless resin. R_f (**11a**): 0.47 (hexanes/EtOAc 90 : 10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 9 H), 2.74 (ddd, *J* = 14.4, 7.8, 0.7 Hz, 1 H), 2.75 (d, *J* = 5.9 Hz, 1 H), 3.06 (dd, *J* = 14.5, 4.3 Hz, 1 H), 4.01 (ddd, *J* = 7.8, 5.9, 4.4 Hz, 1 H), 5.12 (d, *J* = 1.2 Hz, 1 H), 5.31 (m, 1 H), 7.11 (ddd, *J* = 7.5, 7.5, 1.1 Hz, 1 H), 7.16 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.22 (dd, *J* = 7.6, 1.5 Hz, 1 H), 7.33 (ddd, *J* = 8.0, 8.0, 1.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0, 41.7, 69.2, 82.5, 118.3, 119.1, 124.8, 128.8, 130.8, 133.9, 137.0, 143.1, 173.7 ppm. HRMS (CI) *m*/*z* calcd for $C_{15}H_{19}NO_3$ $[M - N_2]^+$: 261.1359. Found: 261.1366.

Diethyl 2-[2-(2-azidophenyl)allyl]malonate (11b). According to the general procedure for diazotation/azidation **10a** (107 mg, (0.367 mmol) was reacted with $NaNO_2$ (41 mg, 0.588 mmol) and NaN_3 (38 mg, 0.588 mmol). Automated flash chromatography (hexanes/EtOAc 100 : 0 to 90 : 10) afforded azide **11b** (104 mg, 0.328 mmol, 89%) as a colorless oil. R_f (**11b**): 0.25 (hexanes/EtOAc 90 : 10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 6 H), 3.08 (m, 2 H), 3.35 (t, *J* = 7.5 Hz, 1 H), 4.15 (q, *J* = 7.1 Hz, 4 H), 5.03 (m, 1 H), 5.25 (m, 1 H), 7.07–7.16 (m, 3 H), 7.32 (ddd, *J* = 8.0, 7.1, 1.9 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 35.8, 50.9, 61.4, 118.0, 118.3, 124.7, 128.9, 130.8, 133.2, 137.1, 144.0, 168.8 ppm. HRMS (CI) *m*/*z* calcd for $C_{16}H_{19}NO_4$ $[M - N_2]^+$: 289.1309. Found: 289.1308.

2-[2-(2-Azidophenyl)allyl]isoindoline-1,3-dione (11c). According to the general procedure for diazotation/azidation **10a** (20 mg, 71.9 μmol) was reacted with $NaNO_2$ (7.9 mg, 0.115 mmol) and NaN_3 (7.5 mg, 0.115 mmol). Column chromatography (hexanes/EtOAc 90 : 10) afforded azide **11c** (15 mg, 49 μmol, 69%) as a colorless solid, m.p. 88–89 °C. R_f (**11c**): 0.23 (hexanes/EtOAc 90 : 10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.67 (s, 2 H), 5.17 (d, *J* = 0.7 Hz, 1 H), 5.33 (d, *J* = 0.7 Hz, 1 H), 7.05 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.15 (dd, *J* = 8.0, 0.6 Hz, 1 H), 7.18 (dd, *J* = 7.6, 1.5 Hz, 1 H), 7.31 (ddd, *J* = 8.0, 8.0, 1.6 Hz, 1 H), 7.70 (m, 2 H), 7.82 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.4, 117.2, 118.2, 123.3, 124.7, 129.2, 130.7, 131.7, 132.0, 133.9, 137.6, 141.8, 167.8 ppm. HRMS (CI) *m*/*z* calcd for $C_{17}H_{11}N_2O_2$ $[M - N_2 - H]^+$: 275.0815. Found: 275.0833.

General procedure for the photocyclization of 2-azidostyrenes

The corresponding azide was dissolved in MeCN (10 mL mmol^{-1}) in a round bottom flask, which was then wrapped with aluminium foil and irradiated with an UV-LED lamp at 25% (6.25 W cm^{-2}) of the maximum irradiance for the specified time at room temperature under laboratory atmosphere. The solvent was removed *in vacuo* and the residue was purified by (automated) flash chromatography.

***tert*-Butyl (*N*-benzoyl)-tryptophanate (7a).** According to the general procedure for photocylization azide **6a** (41 mg, 0.104 mmol) was irradiated for 9.5 h. Automated flash chromatography (hexanes/EtOAc 100 : 0 to 70 : 30) afforded tryptophan **7a** (31 mg, 85.1 μmol, 82%) as a colorless solid, m.p. 125–126 °C. R_f (**7a**): 0.22 (hexanes/EtOAc 70 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H), 3.39 (dd, *J* = 14.9, 5.2 Hz, 1 H), 3.45 (dd, *J* = 14.9, 5.6 Hz, 1 H), 5.06 (ddd, *J* = 7.6, 5.4, 5.4 Hz, 1 H), 6.72 (d, *J* = 7.6 Hz, 1 H), 7.03–7.08 (m, 2 H), 7.17 (m, 1 H), 7.33–7.39 (m, 3 H), 7.47 (m, 1 H), 7.61 (d, *J* = 7.9 Hz, 1 H), 7.69 (m, 2 H), 8.25 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.6, 28.0, 53.9, 82.3, 110.4, 111.1, 119.0, 119.5, 122.1, 122.7, 127.0, 127.9, 128.5, 131.5, 134.1, 136.0, 166.9, 171.1 ppm. HRMS (CI) *m*/*z* calcd for $C_{22}H_{24}N_2O_3$ $[M]^+$: 364.1781. Found: 364.1788.

***tert*-Butyl (*N*-trifluoroacetyl)-tryptophanate (8a).** According to the general procedure for photocylization azide **3a** (79 mg, 0.206 mmol) was irradiated for 12 h. Automated flash chromatography (hexanes/EtOAc 100 : 0, 80 : 20) afforded tryptophan **7a** (55 mg, 0.154 mmol, 75%) as an off-white solid, m.p. 130–132 °C. R_f (**8a**): 0.26 (hexanes/EtOAc 80 : 20). Small amounts of azide **3a** (6 mg, 16 μmol, 8%) were recovered. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (s, 9 H), 3.39 (m, 2 H), 4.83 (m, 1 H), 6.92 (d, *J* = 6.5 Hz, 1 H), 7.00 (d, *J* = 2.0 Hz, 1 H), 7.15 (dd, *J* = 7.2, 7.2 Hz, 1 H), 7.23 (dd, *J* = 7.2, 7.2 Hz, 1 H), 7.36 (d, *J* = 8.1 Hz, 1 H), 7.58 (d, *J* = 7.9 Hz, 1 H), 8.19 (bs, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.1, 27.9, 53.9, 83.4, 109.3, 111.3, 115.6 (d, J_F = 287.8 Hz), 118.8, 119.8, 122.4, 122.8, 127.5, 136.1, 156.7 (d, J_F = 37.4 Hz), 169.4 ppm. HRMS (CI) *m*/*z* calcd for $C_{17}H_{19}F_3N_2O_3$ $[M]^+$: 356.1342. Found: 356.1346.

***tert*-Butyl 2-hydroxy-3-(1*H*-indol-3-yl)propanoate (12a).** According to the general procedure for photocylization azide **11a** (14 mg, 48.4 μmol) was irradiated for 7.5 h. Flash chromatography (hexanes/EtOAc 80 : 20) afforded indole **12a** (9.5 mg, 36.4 μmol, 75%) as a colorless resin. R_f (**12a**): 0.21 (hexanes/EtOAc 80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 9 H), 2.93 (d, *J* = 3.6 Hz, 1 H), 3.14 (dd, *J* = 14.9, 6.2 Hz, 1 H), 3.26 (dd, *J* = 14.9, 4.2 Hz, 1 H), 4.41 (m, 1 H), 7.11–7.21 (m, 3 H), 7.34 (d, *J* = 8.0 Hz, 1 H), 7.66 (d, *J* = 7.8 Hz, 1 H), 8.05 (bs, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.9, 30.0, 71.0, 82.4, 110.8, 111.0, 119.1, 119.3, 122.0, 122.9, 127.8, 136.0, 173.7 ppm. HRMS (CI) *m*/*z* calcd for $C_{15}H_{19}NO_3$ $[M]^+$: 261.1359. Found: 261.1361.

Diethyl 2-[(1*H*-indol-3-yl)methyl]malonate (12b). According to the general procedure for photocylization azide **11b** (75 mg, 0.236 mmol) was irradiated for 12 h. Flash chromatography (hexanes/EtOAc 80 : 20) afforded indole **12b** (59 mg, 0.204 mmol, 86%) as an off-white solid, m.p.: 62–64 °C). R_f (**12b**): 0.18 (hexanes/EtOAc 80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.1 Hz, 6 H), 3.42 (d, *J* = 8.1 Hz, 2 H), 3.80 (t, *J* = 7.6 Hz, 1 H), 4.17 (m, 4 H), 7.02 (d, *J* = 1.2 Hz, 1 H), 7.14 (td, *J* = 7.1, 1.0 Hz, 1 H), 7.20 (m, 1 H), 7.34 (d, *J* = 8.0 Hz, 1 H), 7.63 (d, *J* = 7.9 Hz, 1 H), 8.16 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 24.5, 53.0, 61.4, 111.1, 112.0, 118.5, 119.3,

122.0, 122.5, 127.0, 136.1, 169.3 ppm. HRMS (CI) *m*/*z* calcd for $C_{16}H_{19}NO_4$ $[M]^+$: 289.1309. Found: 289.1313.

2-[(1*H*-Indol-3-yl)methyl]isoindoline-1,3-dione (20). According to the general procedure for photocylizations azide **11c** (14 mg, 46.0 μmol) was irradiated for 6 h. Automated flash chromatography (hexanes/EtOAc 100 : 0 to 80 : 20) afforded indole **12c** (9.8 mg, 35.5 μmol, 77%) as a colorless solid, m.p. 180–182 °C. R_f (**12c**): 0.15 (hexanes/EtOAc 80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.03 (s, 2 H), 7.14–7.21 (m, 2 H), 7.34 (m, 1 H), 7.40 (d, J = 2.5 Hz, 1 H), 7.65 (m, 2 H), 7.80 (m, 2 H), 7.94 (m, 1 H), 8.14 (bs, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.6, 111.0, 111.4, 119.4, 120.0, 122.3, 123.1, 125.1, 126.5, 132.2, 133.8, 135.9, 168.2 ppm. HRMS (CI) *m*/*z* calcd for $C_{17}H_{13}O_2N_2$ $[M + H]^+$: 277.0972. Found: 277.0977.

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References

1 (*a*) W. Gul and M. T. Hamann, *Life Sci.*, 2005, **78**, 442–453; (*b*) C. V. Galliford and K. A. Scheidt, *Angew. Chem.*, 2007, **119**, 8902–8912, (*Angew. Chem., Int. Ed.*, 2007, **46**, 8748–8758); (*c*) A. J. Kochanowska-Karamyan and M. T. Harmann, *Chem. Rev.*, 2010, **110**, 4489–4497; (*d*) S. M. Bronner, G. Y. J. Im and N. K. Garg, in *Heterocycles in Natural Product Synthesis*, ed. K. C. Majumdar and S. K. Chattopadhyay, Wiley-VCH, Weinheim, 2011, pp. 221–265.

2 D. Jakubczyk, J. Z. Cheng and S. E. O'Connor, *Nat. Prod. Rep.*, 2014, **31**, 1328–1338.

3 (*a*) C. D. Murphy, *Nat. Prod. Rep.*, 2006, **23**, 147–152; (*b*) T. Rauhut and E. Glawischnig, *Phytochemistry*, 2009, **70**, 1638–1644; (*c*) M. S. Pedras, E. E. Yaya and E. Glawischnig, *Nat. Prod. Rep.*, 2011, **28**, 1381–1405; (*d*) W. Xu, D. J. Gavia and Y. Tang, *Nat. Prod. Rep.*, 2014, **31**, 1474–1487.

4 N. Fusetani and S. Matsunaga, *Chem. Soc. Rev.*, 1963, **93**, 1793–1808.

5 (*a*) B. Kunze, R. Jansen, F. Sasse, G. Höfle and H. Reichenbach, *J. Antibiot.*, 1995, **48**, 1262–1266; (*b*) R. Jansen, B. Kunze, H. Reichenbach and G. Höfle, *Liebigs Ann.*, 1996, 285–290.

6 (*a*) W. D. Clark, T. Corbett, F. Valeriote and P. Crews, *J. Am. Chem. Soc.*, 1997, **119**, 9285–9286; (*b*) B. K. Rubio, S. J. Robinson, C. E. Avalos, F. A. Valeriote, N. J. de Voogd and P. Crews, *J. Nat. Prod.*, 2008, **71**, 1475–1478; (*c*) J. M. Garcia, S. S. Curzon, K. R. Watts and J. P. Konopelski, *Org. Lett.*, 2012, **14**, 2054–2057.

7 (*a*) R. J. Sundberg, *The Chemistry of Indoles*, Academic Press, New York, 1970; (*b*) R. J. Sundberg, *Indoles*, Academic Press, London, 1996; (*c*) G. W. Gribble, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1045–1075; (*d*) S. Cacchi and G. Fabrizi, *Chem. Rev.*, 2005, **105**, 2873–2920; (*e*) G. R. Humphrey and J. T. Kuethe, *Chem. Rev.*, 2006, **106**, 2875–2911; (*f*) S. Cacchi and G. Fabrizi, *Chem. Rev.*, 2011, **111**, 2215–2283; (*g*) D. F. Taber and P. K. Tirunahari, *Tetrahedron*, 2011, **67**, 7195–7210; (*h*) M. Inman and C. J. Moody, *Chem. Sci.*, 2013, **4**, 29–41; (*i*) G. Bartoli, R. Dalpozzo and M. Nardi, *Chem. Soc. Rev.*, 2014, **43**, 4728–4750.

8 Ausgewählte Reviews: (*a*) K. Fujita and R. Yamaguchi, *Synlett*, 2005, 560–571; (*b*) S. Agarwal, S. Caemmerer, S. Filali, W. Froehner, J. Knoell, M. P. Krahl, K. R. Reddy and H.-J. Knoelker, *Curr. Org. Chem.*, 2005, **9**, 1601–1614; (*c*) K. Krüger, A. Tillack and M. Beller, *Adv. Synth. Catal.*, 2008, **350**, 2153–2167; (*d*) J. Barluenga, F. Rodriguez and F. J. Fananas, *Chem. – Asian J.*, 2009, **4**, 1036–1048; (*e*) M. Bandini and A. Eichholzer, *Angew. Chem.*, 2009, **121**, 9786–9824, (*Angew. Chem., Int. Ed.*, 2009, **48**, 9608–9644); (*f*) J. J. Song, J. T. Reeves, D. R. Fandrick, Z. Tan, N. K. Yee and C. H. Senanayake, *ARKIVOC*, 2010, (Part 1), 390–449; (*g*) S. Cacchi, G. Fabrizi and A. Goggiamani, *Org. Biomol. Chem.*, 2011, **9**, 641–652; (*h*) R. Vicente, *Org. Biomol. Chem.*, 2011, **9**, 6469–6480; (*i*) Z. Shi and F. Glorius, *Angew. Chem.*, 2012, **124**, 9354–9356, (*Angew. Chem., Int. Ed.*, 2012, **51**, 9220–9222).

9 (*a*) R. C. Larock and E. K. Yum, *J. Am. Chem. Soc.*, 1991, **113**, 6689–6690; (*b*) R. C. Larock, E. K. Yum and M. D. Refvik, *J. Org. Chem.*, 1998, **63**, 7652–7662.

10 (*a*) L. Ackermann, L. T. Kaspar and C. J. Gschrei, *Chem. Commun.*, 2004, 2824–2825; (*b*) L. Ackermann, R. Sandmann, A. Villar and L. T. Kaspar, *Tetrahedron*, 2008, **64**, 769–777; (*c*) D. Gao and T. G. Back, *Chem. – Eur. J.*, 2012, **18**, 14828–14840.

11 (*a*) L. S. Hegedus, G. F. Allen, J. J. Bozell and E. L. Waterman, *J. Am. Chem. Soc.*, 1978, **100**, 5800–5807; (*b*) L. S. Hegedus, P. M. Winton and S. Varaprath, *J. Org. Chem.*, 1981, **46**, 2215–2221; (*c*) P. J. Harrington and L. S. Hegedus, *J. Org. Chem.*, 1984, **49**, 2657–2662.

12 (*a*) S. Cacchi, G. Fabrizi and A. Goggiamani, *Adv. Synth. Catal.*, 2006, **348**, 1301–1305; (*b*) B. M. Trost and A. McClory, *Angew. Chem.*, 2007, **119**, 2120–2123, (*Angew. Chem., Int. Ed.*, 2007, **46**, 2074–2077); (*c*) Z. Shi, C. Zhang, S. Li, D. Pan, S. Ding, Y. Cui and N. Jiao, *Angew. Chem.*, 2009, **121**, 4642–4646, (*Angew. Chem., Int. Ed.*, 2009, **48**, 4572–4576).

13 (*a*) C. Ma, X. Liu, S. Yu, S. Zhao and J. M. Cook, *Tetrahedron Lett.*, 1999, **40**, 657–660; (*b*) C. Ma, X. Liu, X. Li, J. Flippen-Anderson, S. Yu and J. M. Cook, *J. Org. Chem.*, 2001, **66**, 4525–4542; (*c*) H. Zhou, X. Liao and J. M. Cook, *Org. Lett.*, 2004, **6**, 249–252; (*d*) J. Ma, W. Yin, H. Zhou and J. M. Cook, *Org. Lett.*, 2007, **9**, 3491–3494.

14 (*a*) Y. Jia and J. Zhu, *Synlett*, 2005, 2469–2472; (*b*) P. S. Baran, C. A. Guerrero, N. B. Ambhaikar and B. D. Hafensteiner, *Angew. Chem.*, 2005, **117**, 3960–3963, (*Angew. Chem., Int. Ed.*, 2005, **44**, 606–609); (*c*) P. S. Baran, B. D. Hafensteiner, N. B. Ambhaikar, C. A. Guerrero and J. D. Gallagher, *J. Am. Chem. Soc.*, 2006, **128**, 8678–8693; (*d*) Y. Jia and J. Zhu, *J. Org. Chem.*, 2006, **71**, 7826–7834;

(*e*) J. Michaux, P. Retailleau and J.-M. Campagne, *Synlett*, 2008, 1532–1536.

15 C. A. Dacko, N. G. Akhmedov and B. C. G. Söderberg, *Tetrahedron: Asymmetry*, 2008, **19**, 2775–2783.

16 (*a*) M. Gander-Coquoz and D. Seebach, *Helv. Chim. Acta*, 1988, **71**, 224–236; (*b*) L. Zhang and J. M. Finn, *J. Org. Chem.*, 1995, **60**, 5719–5720; (*c*) T. Gan, R. Liu, P. Yu, S. Zhao and J. M. Cook, *J. Org. Chem.*, 1997, **62**, 9298–9304; (*d*) H. D. Jain, C. Zhang, S. Zhou, H. Zhou, J. Ma, X. Liu, X. Liao, A. M. Deveau, C. M. Dieckhaus, M. A. Johnson, K. S. Smith, T. L. Macdonald, H. Kakeya, H. Osada and J. M. Cook, *Bioorg. Med. Chem.*, 2008, **16**, 4626–4651; (*e*) M. Okada, I. Sato, S. J. Cho, Y. Suzuki, M. Ojika, D. Dubnau and Y. Sakagami, *Biosci., Biotechnol., Biochem.*, 2004, **68**, 2374–2387; (*f*) P. Zhang, R. Liu and J. M. Cook, *Tetrahedron Lett.*, 1995, **36**, 9133–9136; (*g*) S. Bittner, R. Scherzer and E. Harlev, *Amino Acids*, 2007, **33**, 19–42; (*h*) C. R. Edwankar, R. V. Edwankar, O. A. Namjoshi, X. Liao and J. M. Cook, *J. Org. Chem.*, 2013, **78**, 6471–6487.

17 (*a*) U. Schmidt and J. Wild, *Liebigs Ann. Chem.*, 1985, 1882–1894; (*b*) Y. Yokoyama, T. Matsumoto and Y. Murakami, *J. Org. Chem.*, 1995, **60**, 1486–1487; (*c*) Y. Yokoyama, H. Hikawa, M. Mitsuhashi, A. Uyama, Y. Hiroki and Y. Murakami, *Eur. J. Org. Chem.*, 2004, 1244–1253.

18 M. Tanaka, H. Hikawa and Y. Yokoyama, *Tetrahedron*, 2011, **67**, 5897–5901.

19 M. Terada, K. Moriya, K. Kanomata and K. Sorimachi, *Angew. Chem.*, 2011, **123**, 12794–12798, (*Angew. Chem., Int. Ed.*, 2011, **50**, 12586–12590).

20 (*a*) Q. Liu, Q. Li, Y. Ma and Y. Jia, *Org. Lett.*, 2013, **15**, 4528–4531; (*b*) S. Preciado, L. Mendive-Tapia, F. Alberico and R. Lavilla, *J. Org. Chem.*, 2013, **78**, 8129–8135; (*c*) H. K. Potukuchi and T. Bach, *J. Org. Chem.*, 2013, **78**, 12263–12267; (*d*) Y. Feng, D. Holte, J. Zoller, S. Umemiya, L. R. Simke and P. S. Baran, *J. Am. Chem. Soc.*, 2015, **137**, 10160–10163.

21 U. Kazmaier, in *Frontiers in Asymmetric Synthesis and Application of alpha-Amino Acids*, ed. Hrsg.: V. A. Soloshonok and K. Izawa, ACS Books, Washington, 2009, pp. 157–176.

22 (*a*) U. Kazmaier, J. Deska and A. Watzke, *Angew. Chem.*, 2006, **118**, 4973–4976, (*Angew. Chem., Int. Ed.*, 2006, **45**, 4855–4858); (*b*) K. Krämer, J. Deska, C. Hebach and U. Kazmaier, *Org. Biomol. Chem.*, 2009, **7**, 103–111; (*c*) S. Datta and U. Kazmaier, *Org. Biomol. Chem.*, 2011, **9**, 872–880; (*d*) S. Datta, A. Bayer and U. Kazmaier, *Org. Biomol. Chem.*, 2012, **10**, 8268–8275; (*e*) U. Kazmaier, A. Bayer and J. Deska, *Synthesis*, 2013, 1462–1468.

23 (*a*) R. Grandel and U. Kazmaier, *Tetrahedron Lett.*, 1997, **38**, 8009–8012; (*b*) R. Grandel, U. Kazmaier and F. Rominger, *J. Org. Chem.*, 1998, **63**, 4524–4528.

24 (*a*) M. Pohlman and U. Kazmaier, *Org. Lett.*, 2003, **5**, 2631–2633; (*b*) M. Pohlman, U. Kazmaier and T. Lindner, *J. Org. Chem.*, 2004, **69**, 6909–6912; (*c*) B. Mendler and U. Kazmaier, *Org. Lett.*, 2005, **7**, 1715–1718.

25 (*a*) U. Kazmaier and F. L. Zumpe, *Angew. Chem.*, 1999, **111**, 1572–1574, (*Angew. Chem., Int. Ed.*, 1999, **38**, 1468–1470); (*b*) U. Kazmaier and F. L. Zumpe, *Angew. Chem.*, 2000, **112**, 805–807, (*Angew. Chem., Int. Ed.*, 2000, **39**, 802–804); (*c*) U. Kazmaier and T. Lindner, *Angew. Chem.*, 2005, **117**, 3368–3371, (*Angew. Chem., Int. Ed.*, 2005, **44**, 3303–3306); (*d*) U. Kazmaier and D. Stolz, *Angew. Chem.*, 2006, **118**, 3143–3146, (*Angew. Chem., Int. Ed.*, 2006, **45**, 3072–3075); (*e*) U. Kazmaier, D. Stolz, K. Krämer and F. Zumpe, *Chem. – Eur. J.*, 2008, **14**, 1322–1329.

26 (*a*) U. Kazmaier, D. Schauß, S. Raddatz and M. Pohlman, *Chem. – Eur. J.*, 2001, **7**, 456–464; (*b*) C. Bukovec, A. O. Wesquet and U. Kazmaier, *Eur. J. Org. Chem.*, 2011, 1047–1056.

27 (*a*) J. Deska and U. Kazmaier, *Angew. Chem.*, 2007, **119**, 4654–4657, (*Angew. Chem., Int. Ed.*, 2007, **46**, 4570–4573); (*b*) J. Deska and U. Kazmaier, *Chem. – Eur. J.*, 2007, **13**, 6204–6211.

28 U. Kazmaier, D. Schauß, M. Pohlman and S. Raddatz, *Synthesis*, 2000, 914–916.

29 (*a*) G. T. Crisp and P. T. Glink, *Tetrahedron Lett.*, 1992, **33**, 4649–4652; (*b*) G. T. Crisp and P. T. Glink, *Tetrahedron Lett.*, 1994, **50**, 3213–3234.

30 (*a*) S. P. H. Mee, V. Lee and J. E. Baldwin, *Angew. Chem.*, 2004, **116**, 1152–1156, (*Angew. Chem., Int. Ed.*, 2004, **43**, 1132–1136); (*b*) S. P. H. Mee, V. Lee and J. E. Baldwin, *Chem. – Eur. J.*, 2005, **11**, 3294–3308.

31 Xi. Han, B. M. Stoltz and E. J. Corey, *J. Am. Chem. Soc.*, 1999, **121**, 7600–7605.

32 K. Barral, A. D. Moorhouse and J. E. Moses, *Org. Lett.*, 2007, **9**, 1809–1811.

33 K. Nakanishi, X. Huang, H. Jiang, Y. Liu, K. Fang, D. Huang, S. K. Choi, E. Katz and M. Eldefrawi, *Bioorg. Med. Chem.*, 1997, **5**, 1969–1988.

34 (*a*) M. Shen, B. E. Leslie and T. G. Driver, *Angew. Chem.*, 2008, **120**, 5134–5137, (*Angew. Chem., Int. Ed.*, 2008, **47**, 5056–5059); (*b*) B. J. Stokes, K. J. Richert and T. G. Driver, *J. Org. Chem.*, 2009, **74**, 6442–6451; (*c*) K. Sun, S. Liu, P. M. Bec and T. G. Driver, *Angew. Chem.*, 2011, **123**, 1740–1744, (*Angew. Chem., Int. Ed.*, 2011, **50**, 1702–1706); (*d*) C. Kong and T. G. Driver, *Org. Lett.*, 2015, **17**, 802–805.

35 E. P. Farney and T. P. Yoon, *Angew. Chem.*, 2014, **126**, 812–816, (*Angew. Chem., Int. Ed.*, 2014, **53**, 793–797).

36 For photochemical indole syntheses using aryl azides see: (*a*) P. A. S. Smith and B. B. Brown, *J. Am. Chem. Soc.*, 1952, **73**, 2435–2437; (*b*) R. J. Sundberg, H. F. Russell, W. V. Ligon Jr. and L.-S. Lin, *J. Org. Chem.*, 1972, **37**, 719–724; (*c*) P. Molina, J. Alcantara and C. Lopez-Leonardo, *Tetrahedron Lett.*, 1995, **36**, 953–956; (*d*) O. Leogane and H. Lebel, *Angew. Chem.*, 2008, **120**, 356–358, (*Angew. Chem., Int. Ed.*, 2008, **47**, 350–352); (*e*) D. R. Bobeck, S. France, C. A. Leverett, F. Sánchez-Cantalejo and A. Padwa, *Tetrahedron Lett.*, 2009, **50**, 3145–3147; X. D. Xia, J. Xuan, Q. Wang, L.-Q. Lu, J. R. Chen and W. J. Xiao, *Adv. Synth. Catal.*, 2014, **356**, 2807–2812.

37 A. Kiefer, D. Gawas and U. Kazmaier, *Eur. J. Org. Chem.*, 2015, 5810–5816.

