Synthese photoschaltbarer Azopeptide

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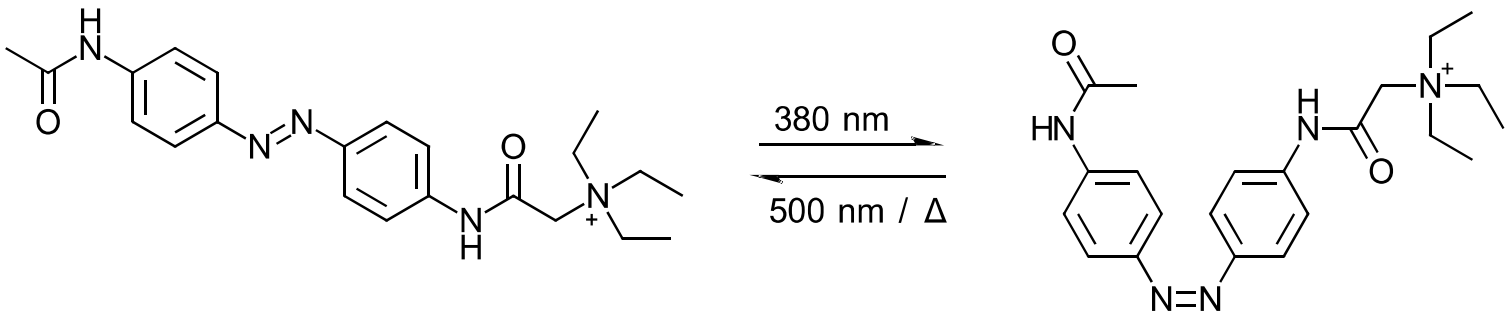
Motivation

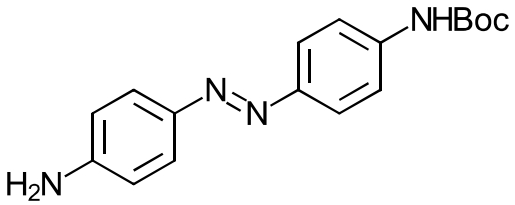


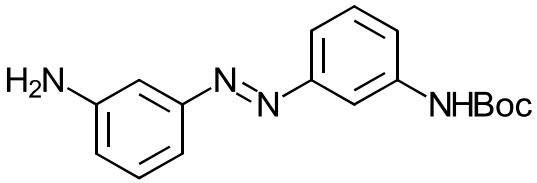
- Kaliumkanäle erlauben Durchtritt von Kaliumionen
- AAQ (Acrylamid-Azo-Tetra-Ammonium) bindet an die Tetraethylammonium-Bindungsstellen in den Kaliumkanälen

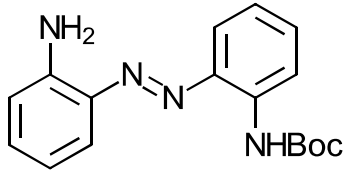
Banghardt, M.; Mourot, A.; Furtin, D. ; Kramer, R.; Trauner, D. *Angew. Chem. Int. Ed.* **2009**, *48,* 9079-9101

1. Synthese von funktionalisierbaren Azo-Benzolen

- Einbau in Peptidketten

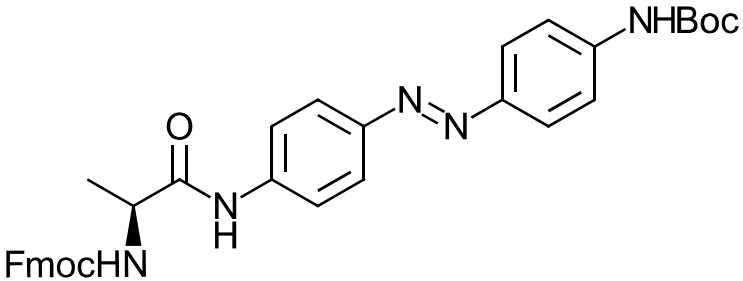




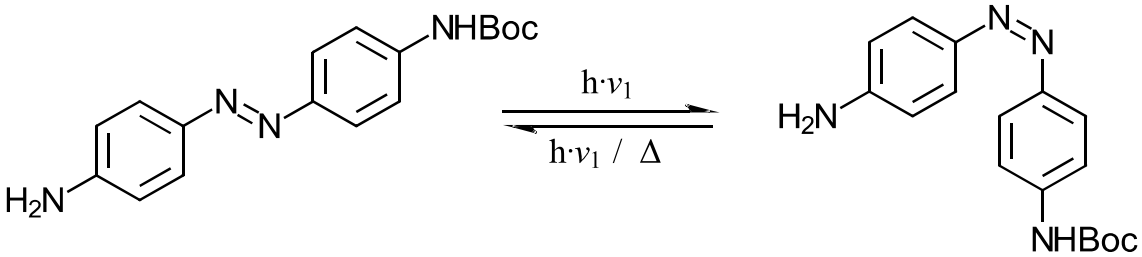


2. Synthese von schaltbaren Azo-Peptiden

- Einbau von Aminosäuren unter typischen Peptidkupplungsbedingungen



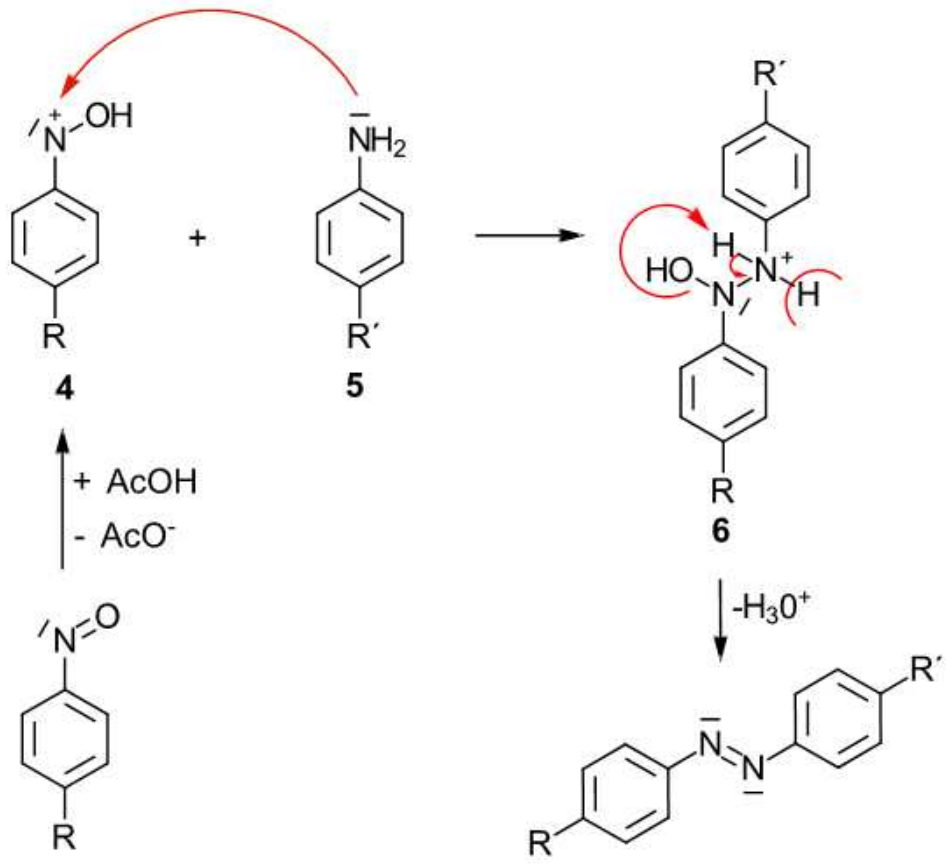
3. Schalten (E/Z bzw. *cis*-/*trans* -Isomerisierung)



4. Herstellen von Katalysatoren auf Basis der Azo-Bausteine

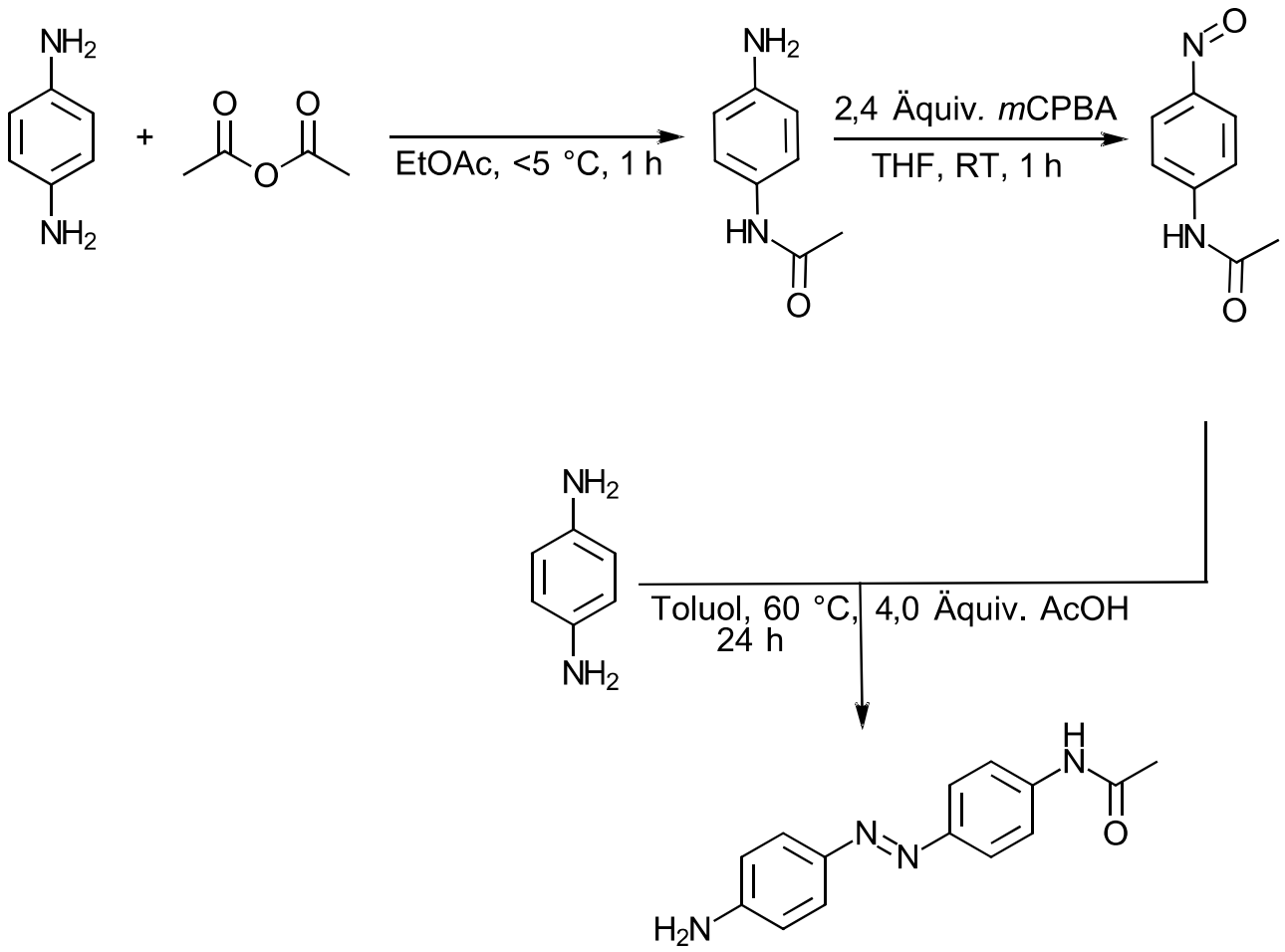
- Verwendung des Motivs π-Methyl-L-Histidin für die chemo- bzw. regioselektive Acylierung von Polyolen wie z.B. Zuckern
- Untersuchungen der Reaktivitäten von E- und Z-Isomer des Katalysators
- Steuerung der Selektivitäten

Mills-Kupplung



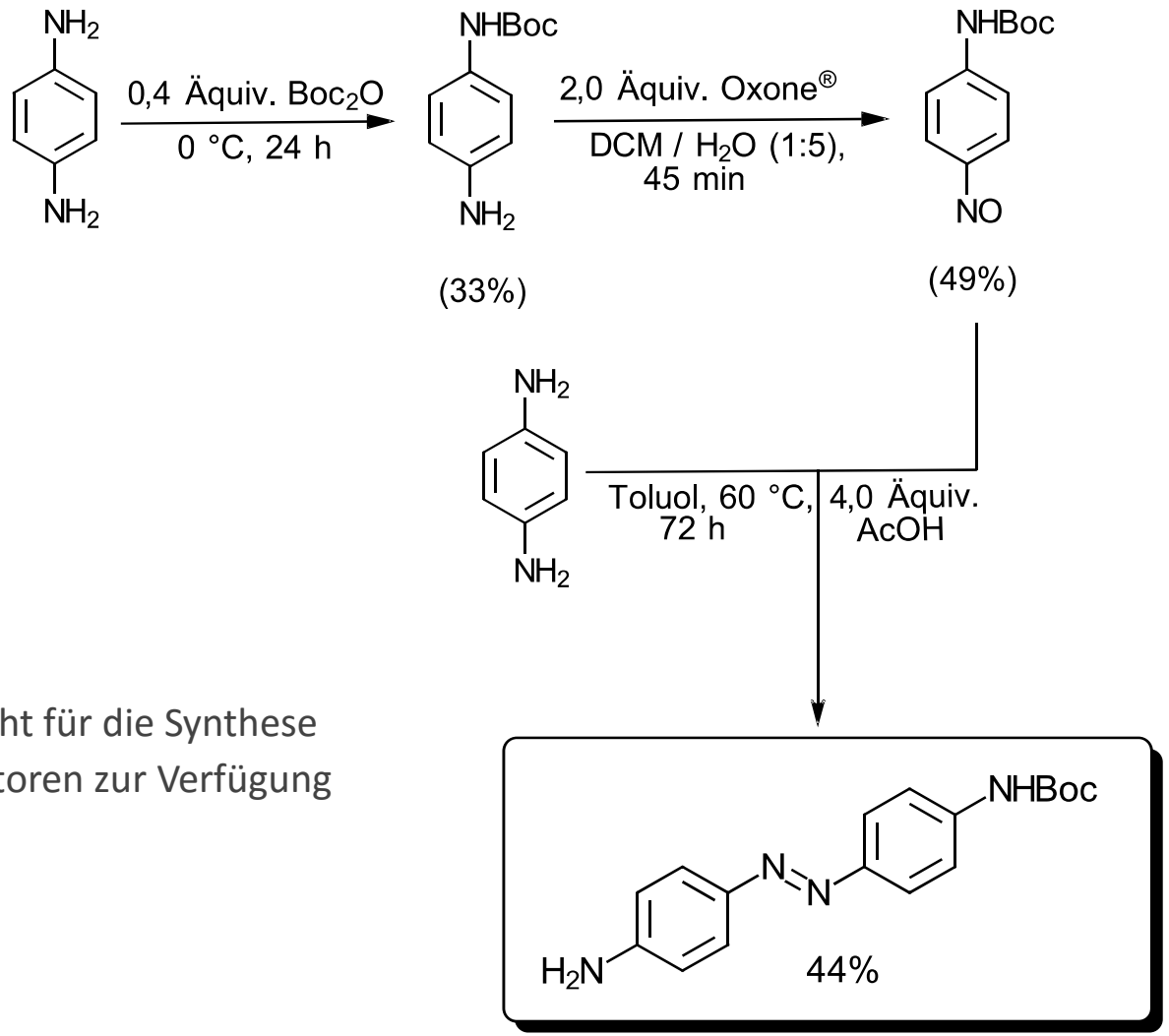
- Bietet ein breites Spektrum an Substitutionsmustern
- Weiteroxidation zur Nitro- und Azoxyverbindung

Modellsystem



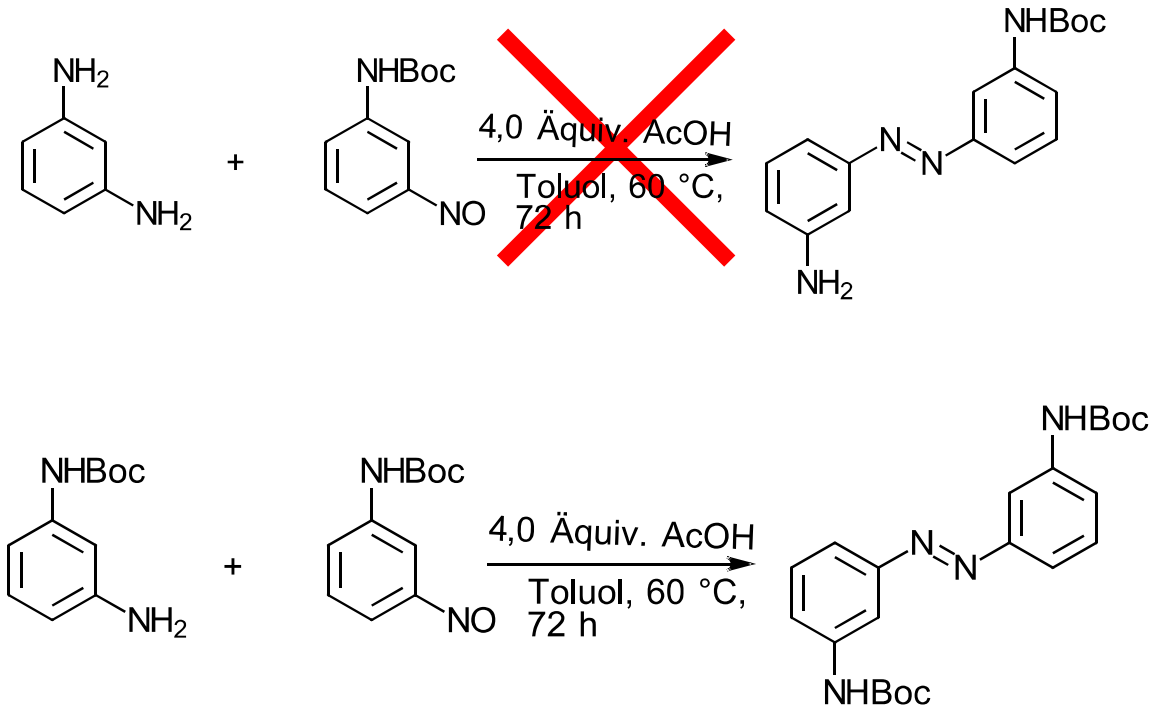
- Direkte Umsetzung der Nitrosospezies notwendig

p-Derivat

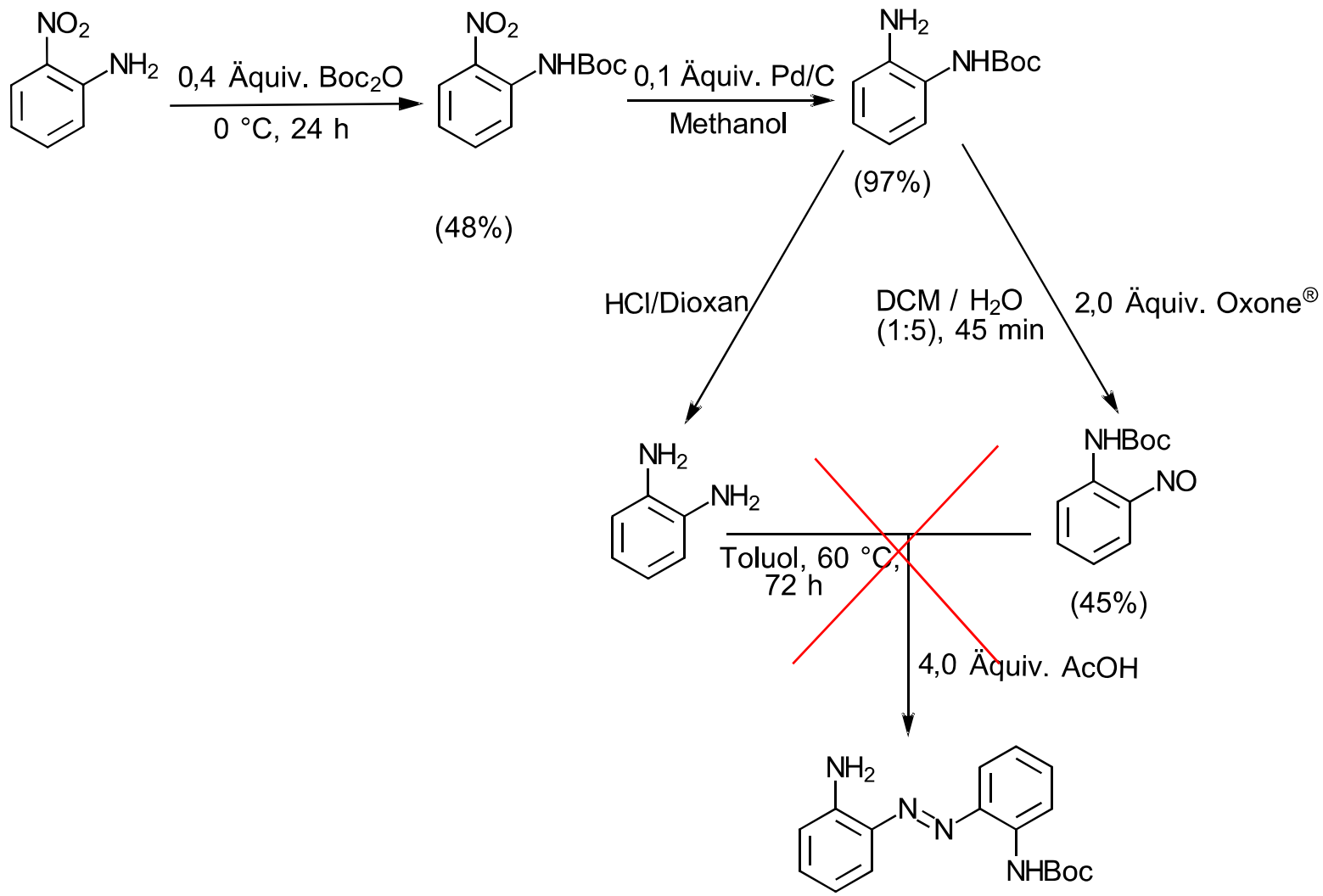


- *p*-Derivat steht für die Synthese von Katalysatoren zur Verfügung

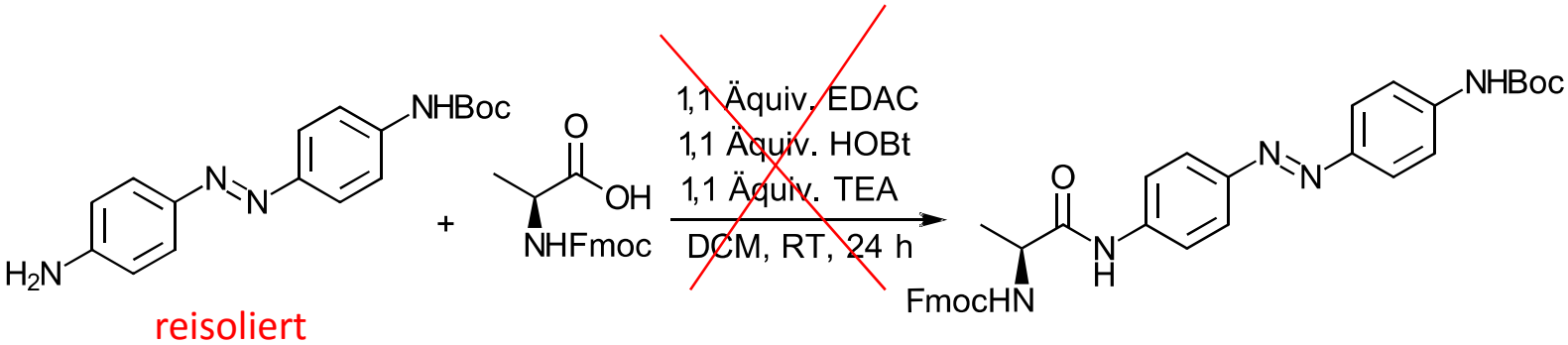
m-Derivat


NH2
NH2
+
NHBoc
NO
4,0 Äquiv. AcOH
Toluol, 60 °C,
72 h
NHBoc
N
N
NH2
NHBoc
NH2
+
NHBoc
NO
4,0 Äquiv. AcOH
Toluol, 60 °C,
72 h
NHBoc
N
N
NHBoc

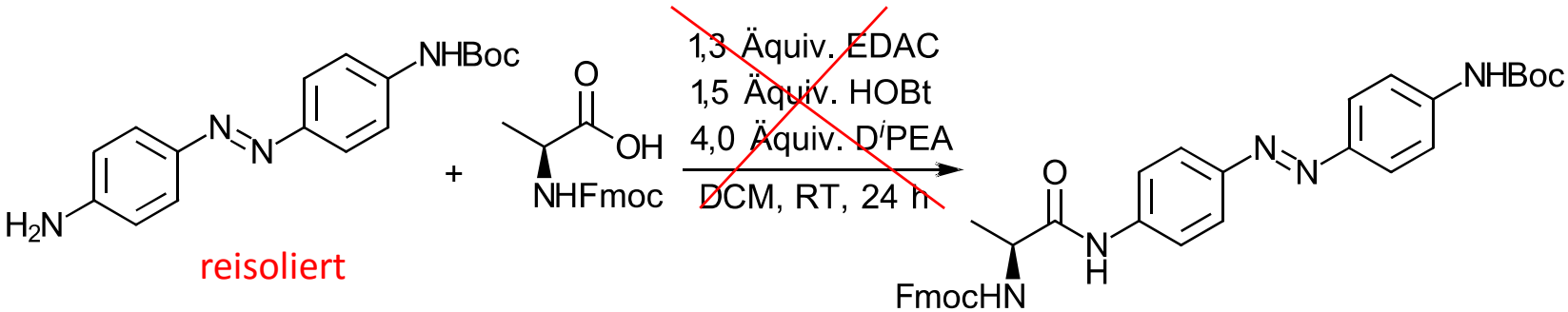
o-Derivat


NO2
NH2
0,4 Äquiv. Boc2O
0 °C, 24 h
NO2
NHBoc
(48%)
0,1 Äquiv. Pd/C
Methanol
NH2
NHBoc
(97%)
HCl/Dioxan
DCM / H2O
(1:5), 45 min
2,0 Äquiv. Oxone®
NH2
NH2
Toluol, 60 °C,
72 h
NHBoc
NO
(45%)
4,0 Äquiv. AcOH
NH2
N
N
NHBoc

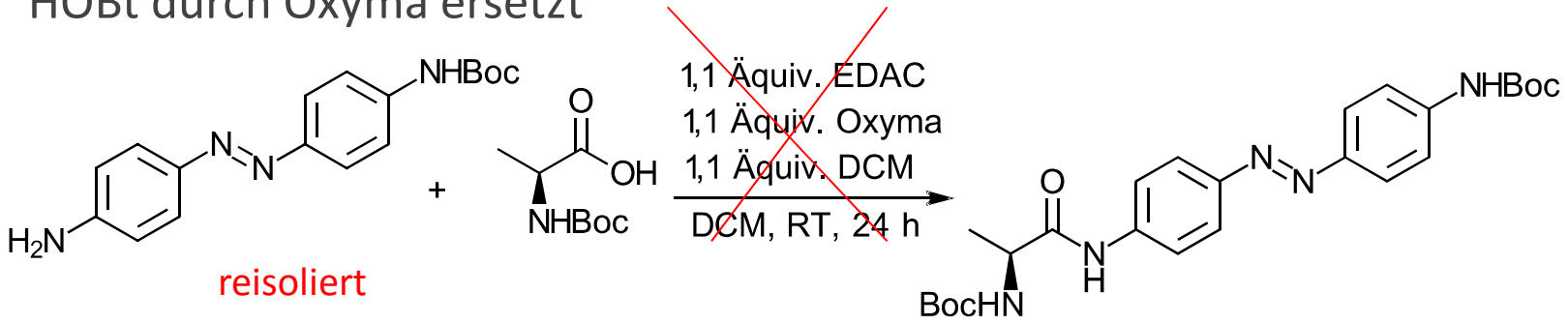
- Testreaktion mit Alanin
- N-Terminus: Fmoc-Schutzgruppe



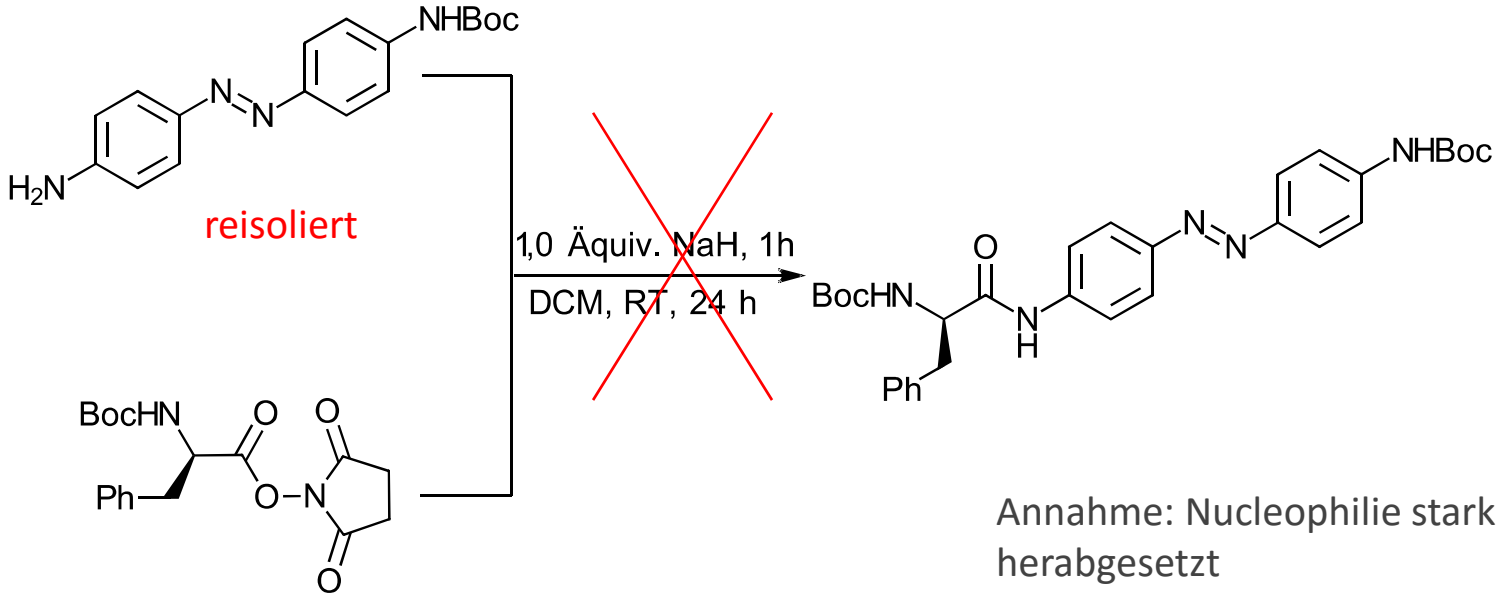
- Verwendung einer stärkeren Base: D^{i}PEA



- HOBt durch Oxyma ersetzt

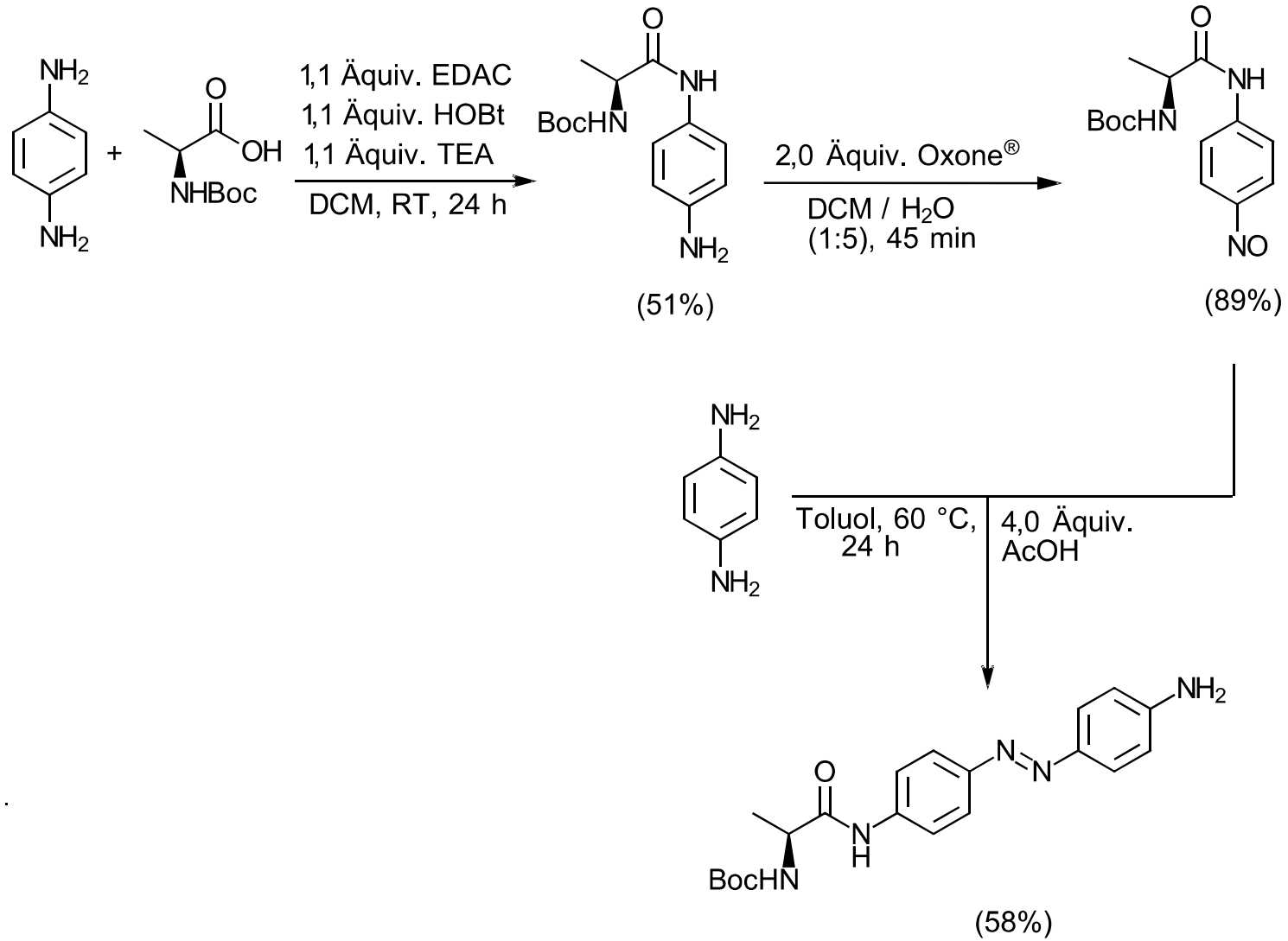


- Direkte Kupplung (NaH und Phenylalaninaktivester)

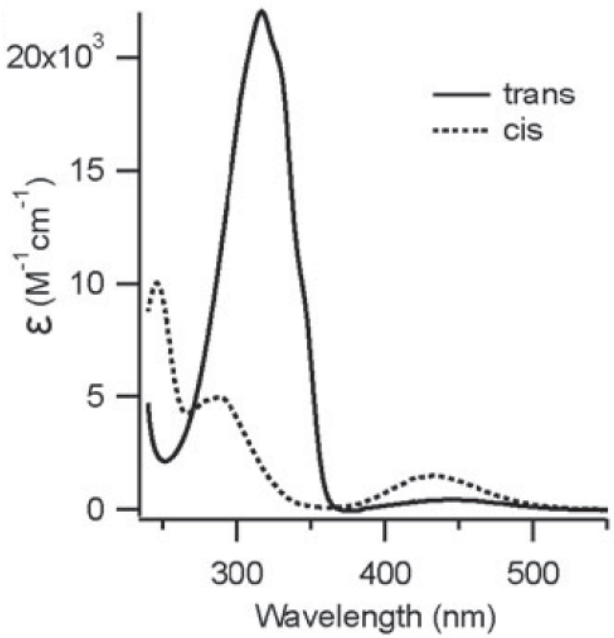


Annahme: Nucleophilie stark herabgesetzt

Alternative Syntheseroute



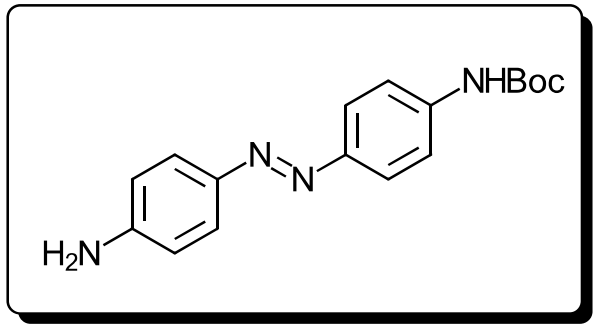
- Typisches Absorptionsspektrum:
  - Zwei charakteristische Absorptionsbanden

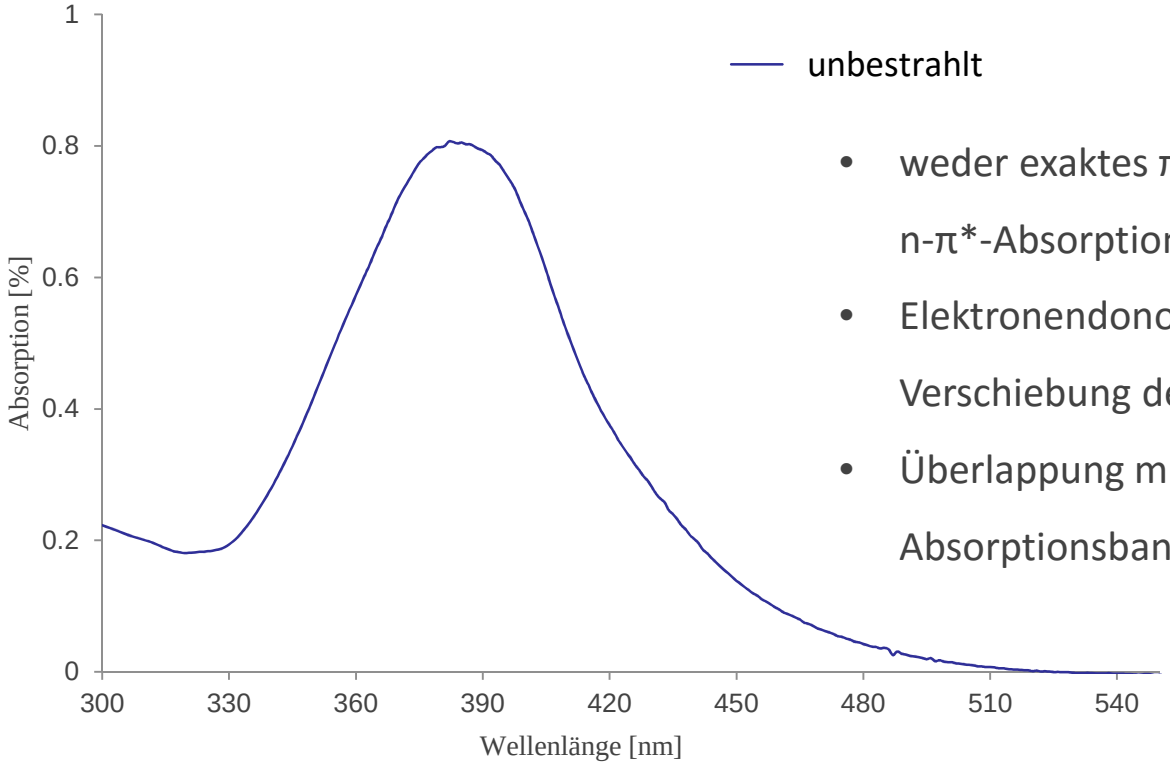


- Kurzwellige, stark ausgeprägte Absorptionsbande entspricht π-π*-Übergang (UV-Bereich)

- Langwellig, wesentlich schwächere Absorptionsbande entspricht n-π*-Übergang (VIS-Bereich)

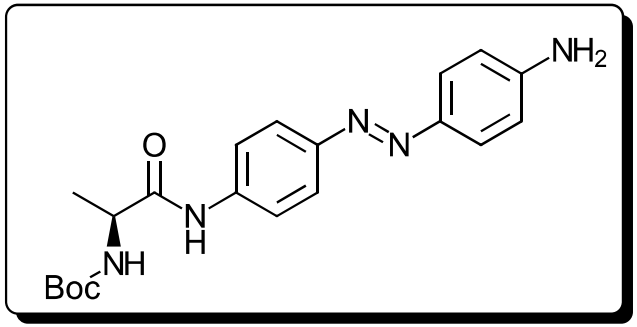
UV-Spektrum

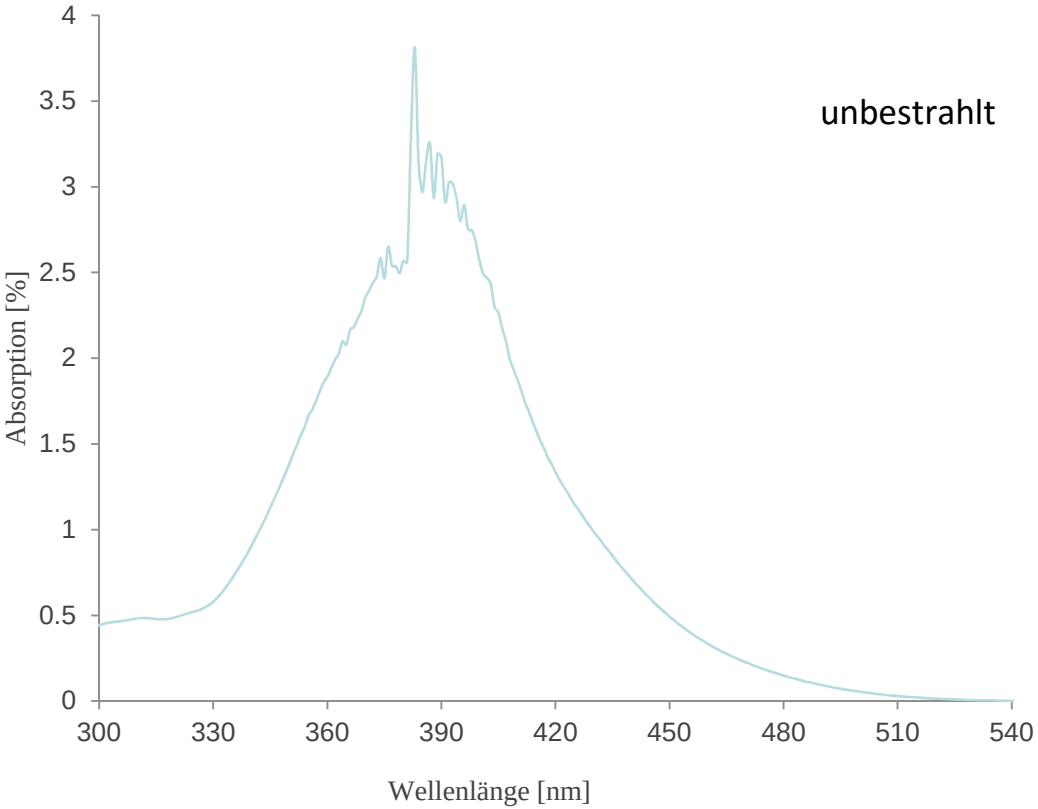




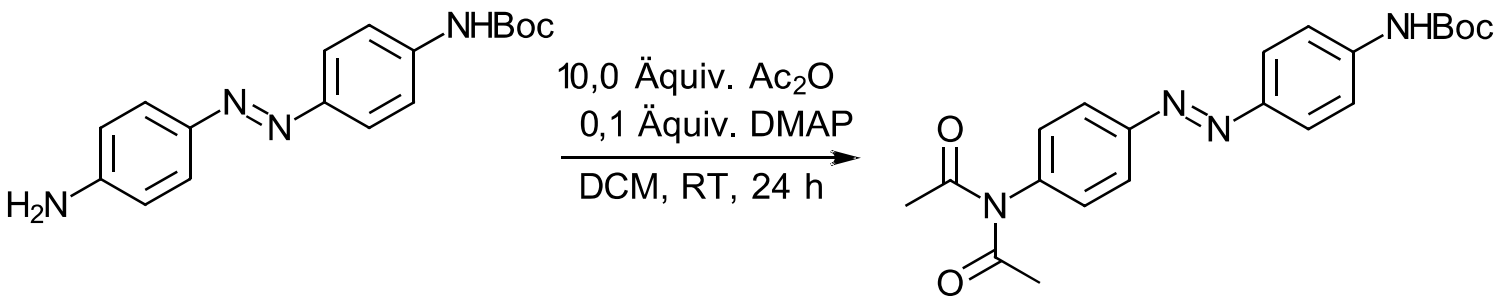
- weder exaktes π-π*- noch ein n-π*-Absorptionsmaximum identifizierbar
- Elektronendonor bewirkt eine bathochrome Verschiebung der π-π*-Absorptionsbande
- Überlappung mit der unveränderten n- π*-Absorptionsbande

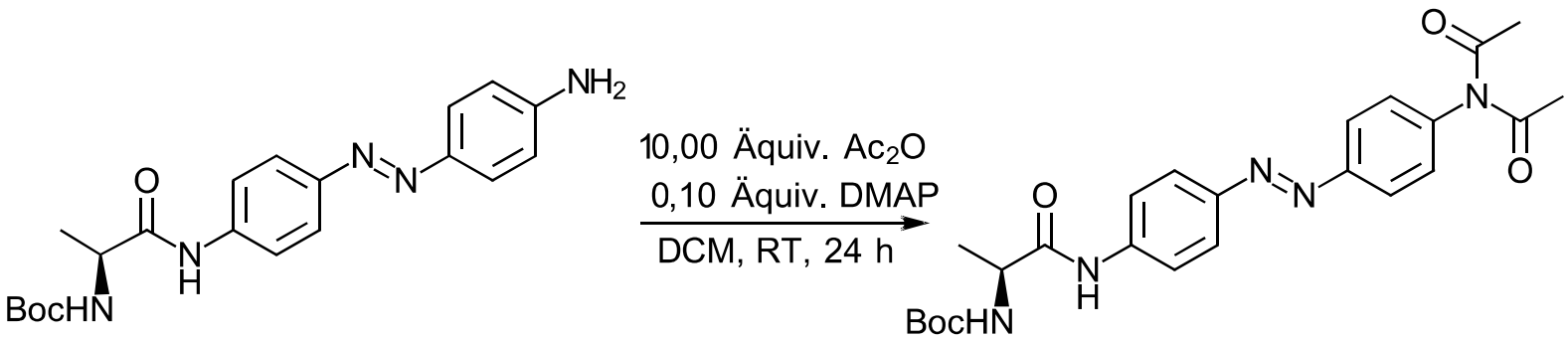
UV-Spektrum


NH2
N
N
O
N
H
NH
Boc

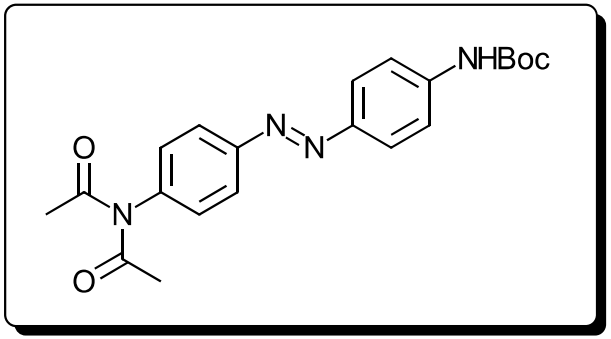

unbestrahlt
Absorption [%]
Wellenlänge [nm]
0
0.5
1
1.5
2
2.5
3
3.5
4
300
330
360
390
420
450
480
510
540

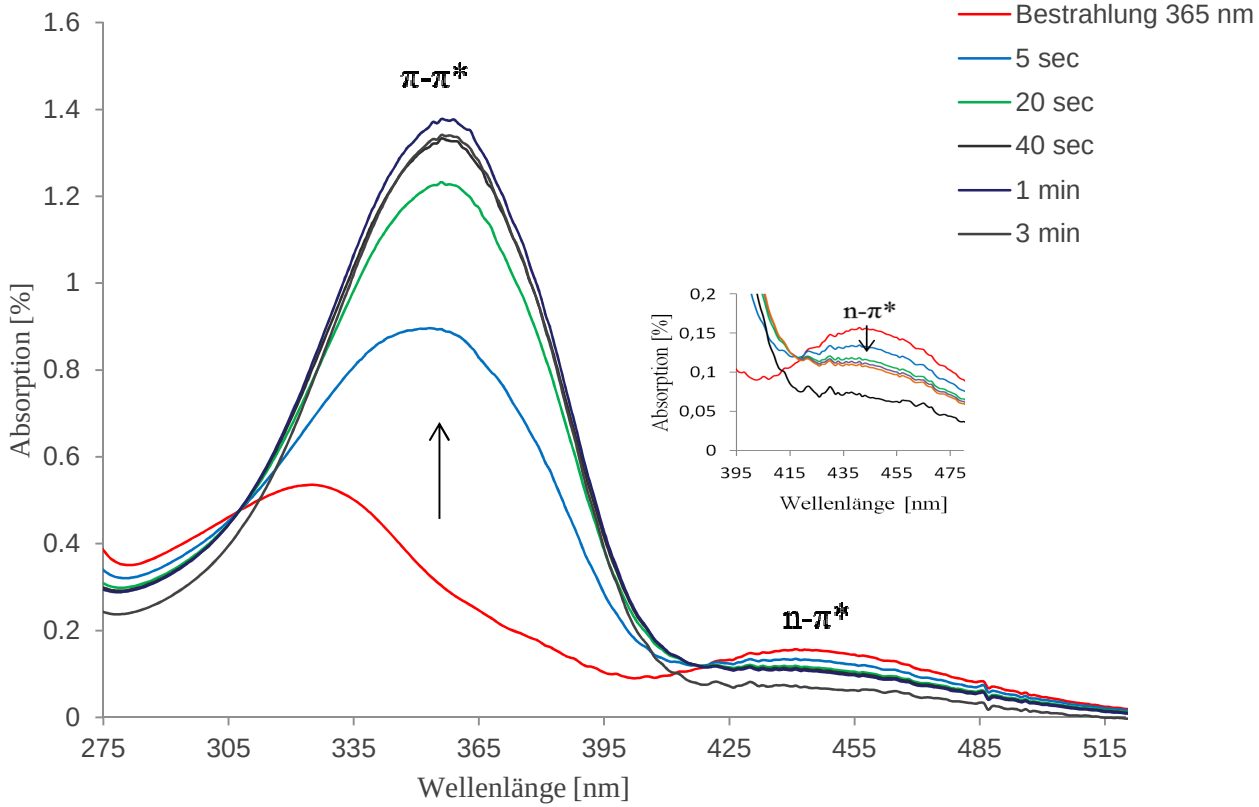
- Ziel: keine Überlappung
- Verkleinerung des chromophoren Systems
  - bewirkt hypsochrome Verschiebung der π-π*-Absorptionsbande



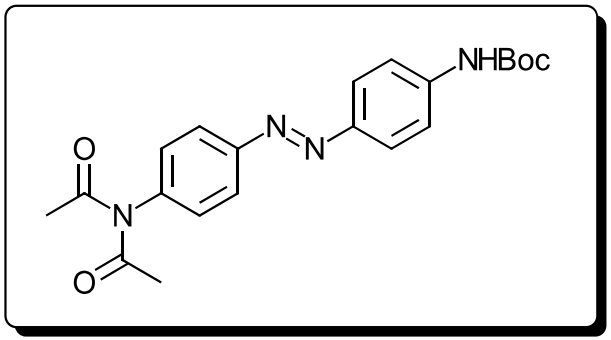


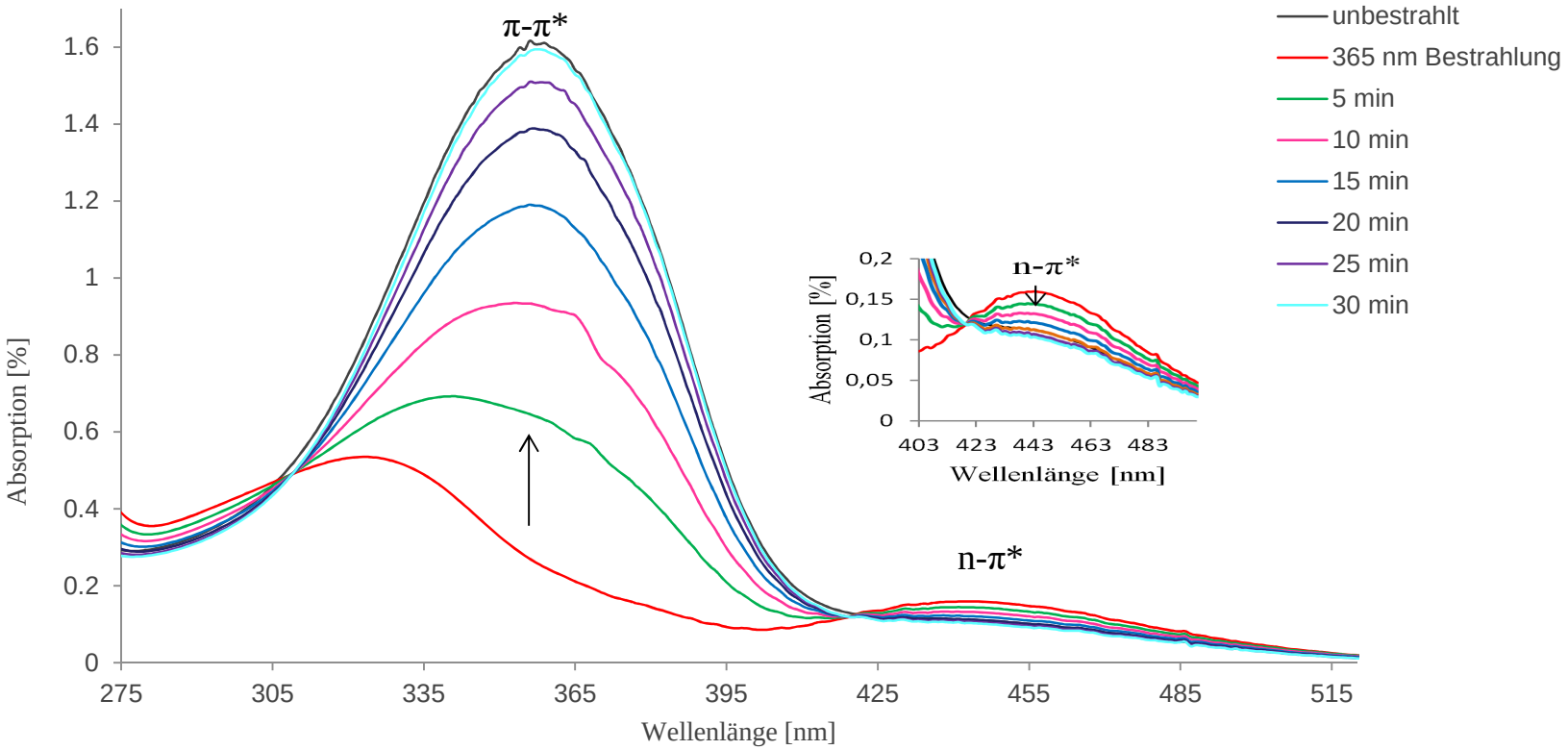
UV-Spektrum nach Acylierung



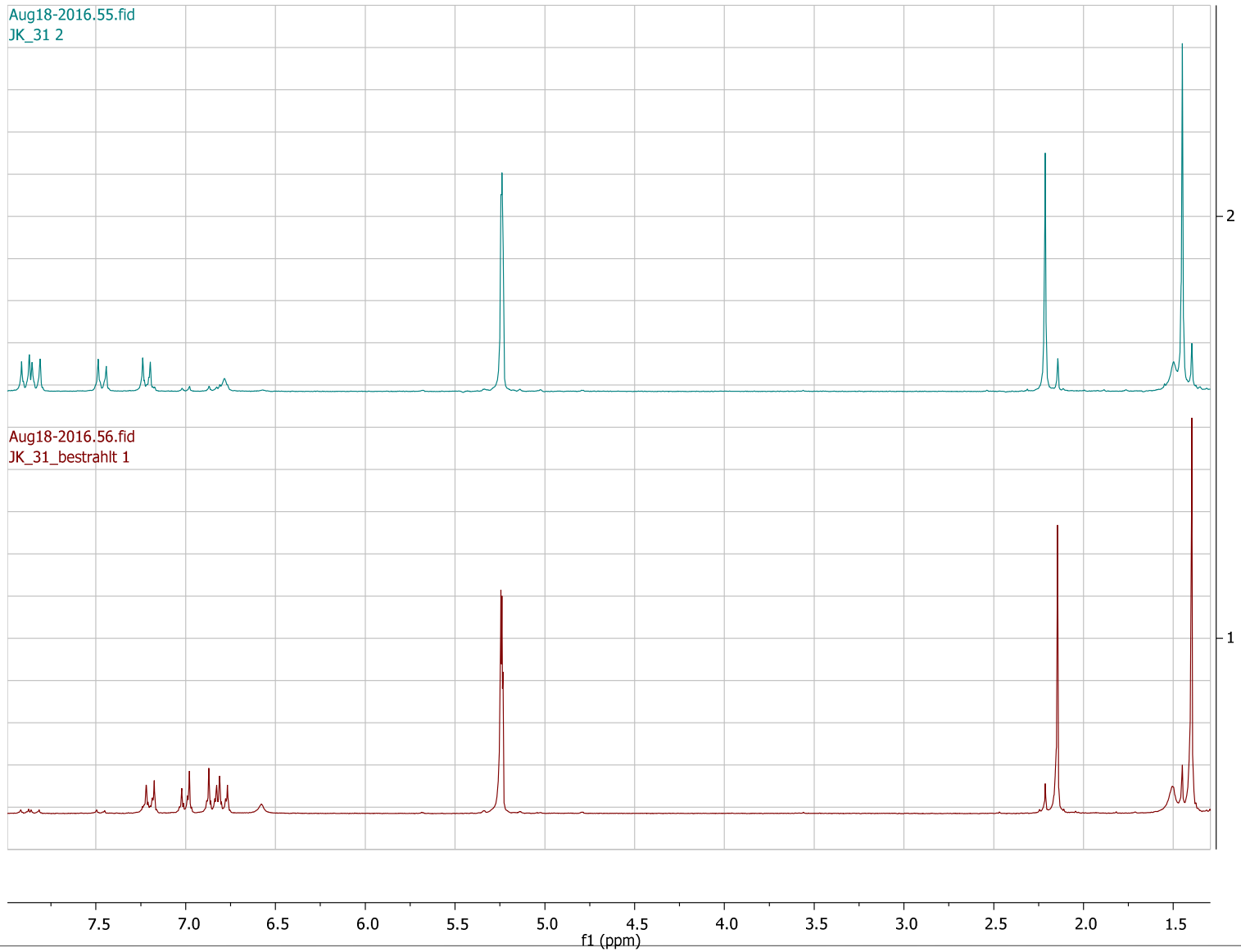


Thermische Relaxation

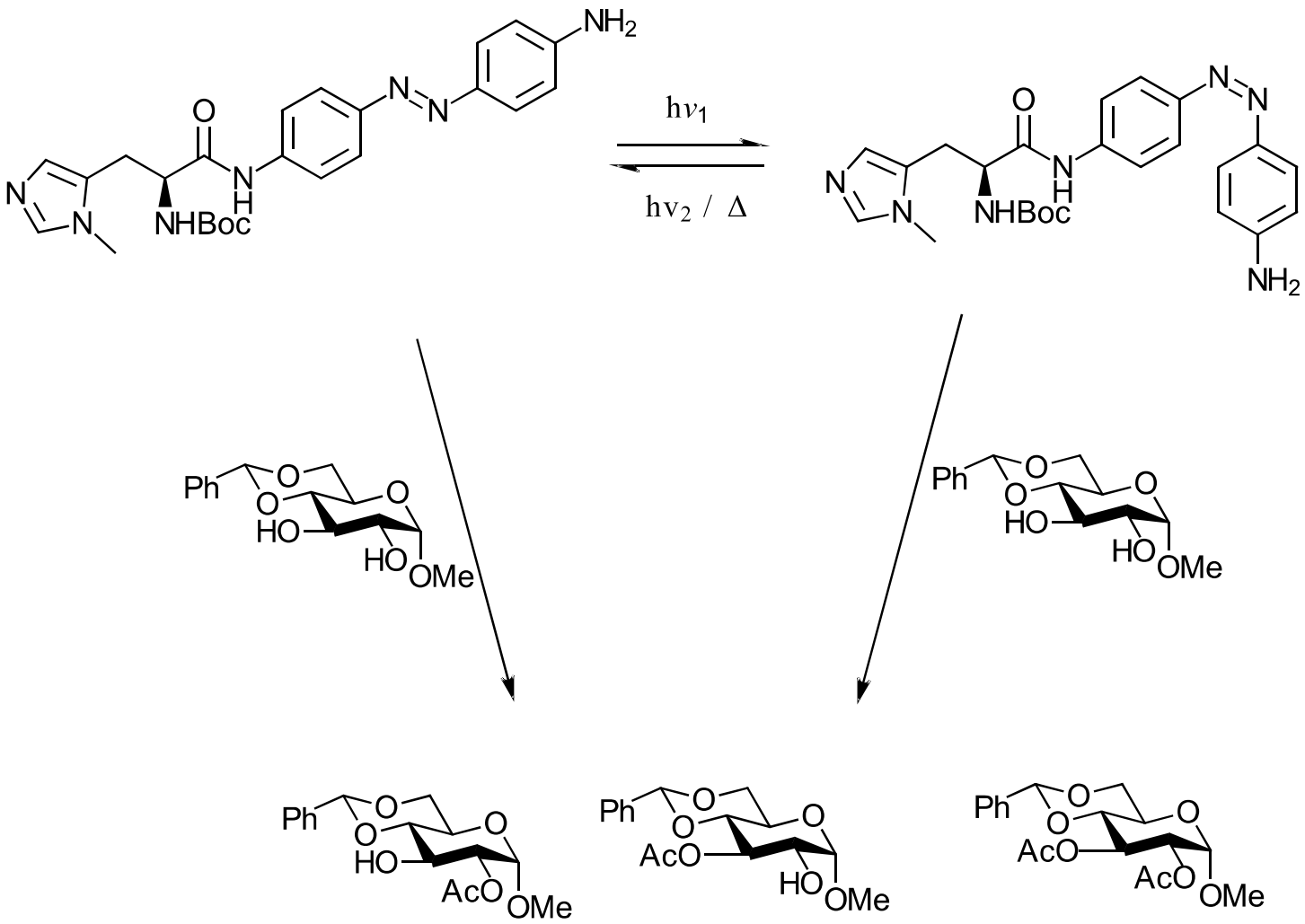




^{1}H-NMR


Aug18-2016.55.fid
JK_31 2
Aug18-2016.56.fid
JK_31_bestrahlt 1
2
1
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

Ausblick



Danksagung

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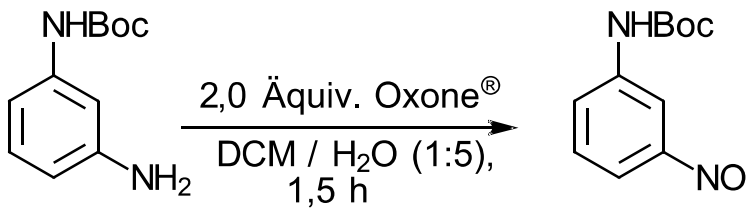
- Dominik Niedek
- Sebastian Ahles und Andreas Heindl (AG Wegner)
- Alexander, Eschi, Jan-Phillip B. , Jan, Raffael
- Christopher und Jaqueline
- AG Schreiner

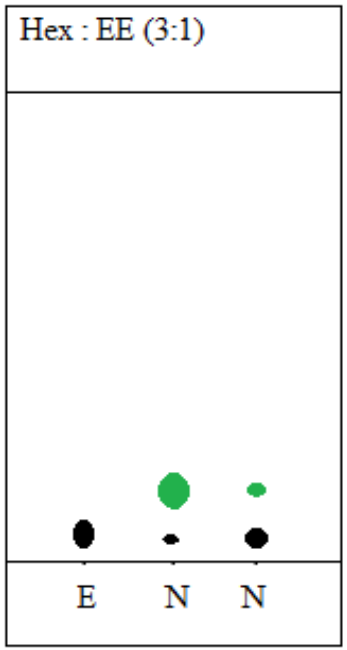
Vielen Dank für Ihre Aufmerksamkeit !

m-Derivat



- Umsetzung der Nitrosoverbindung unter Mills-Bedingungen ohne Zugabe eines Kupplungspartners

- Disproportionierung der Nitrosoverbindung

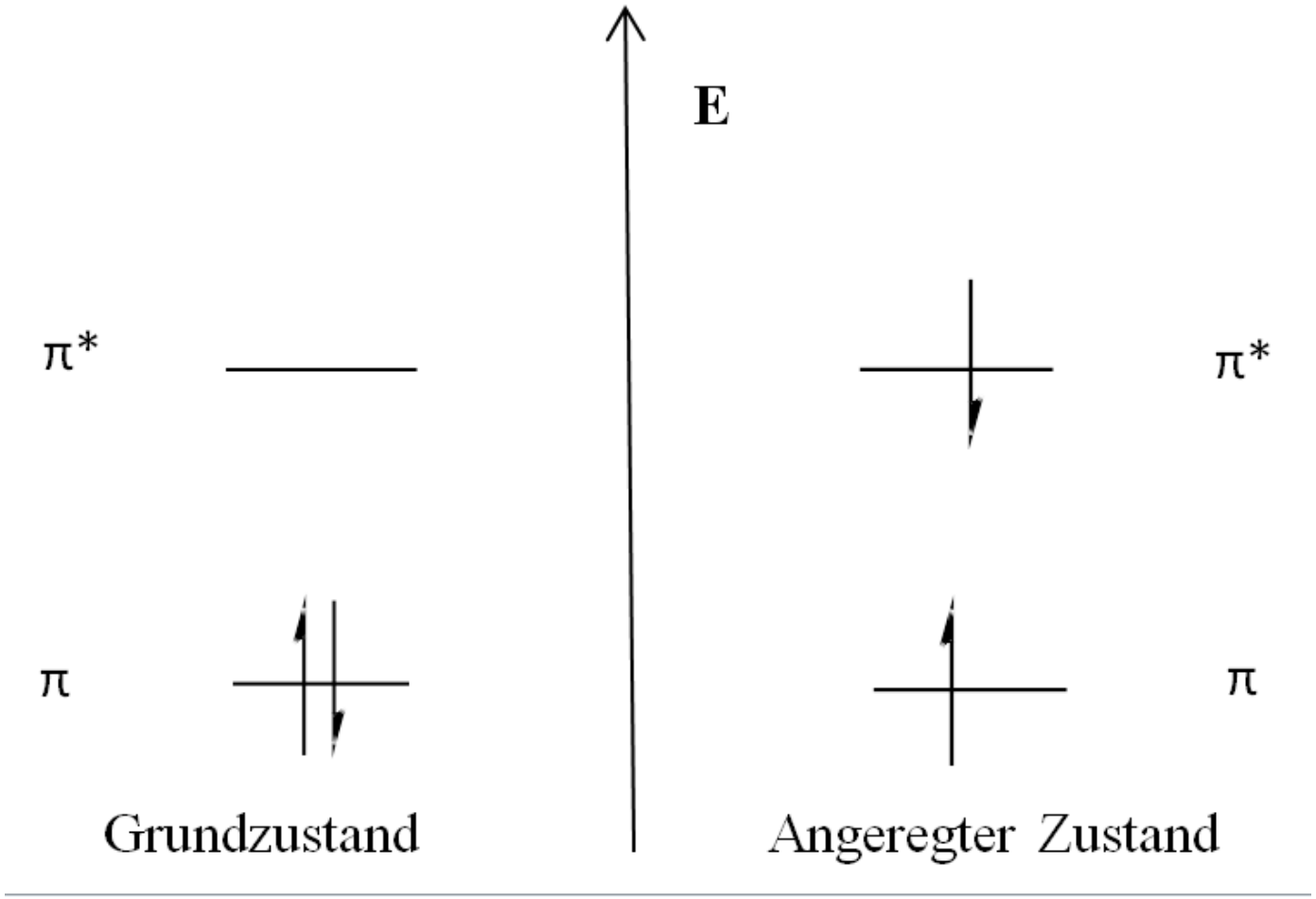


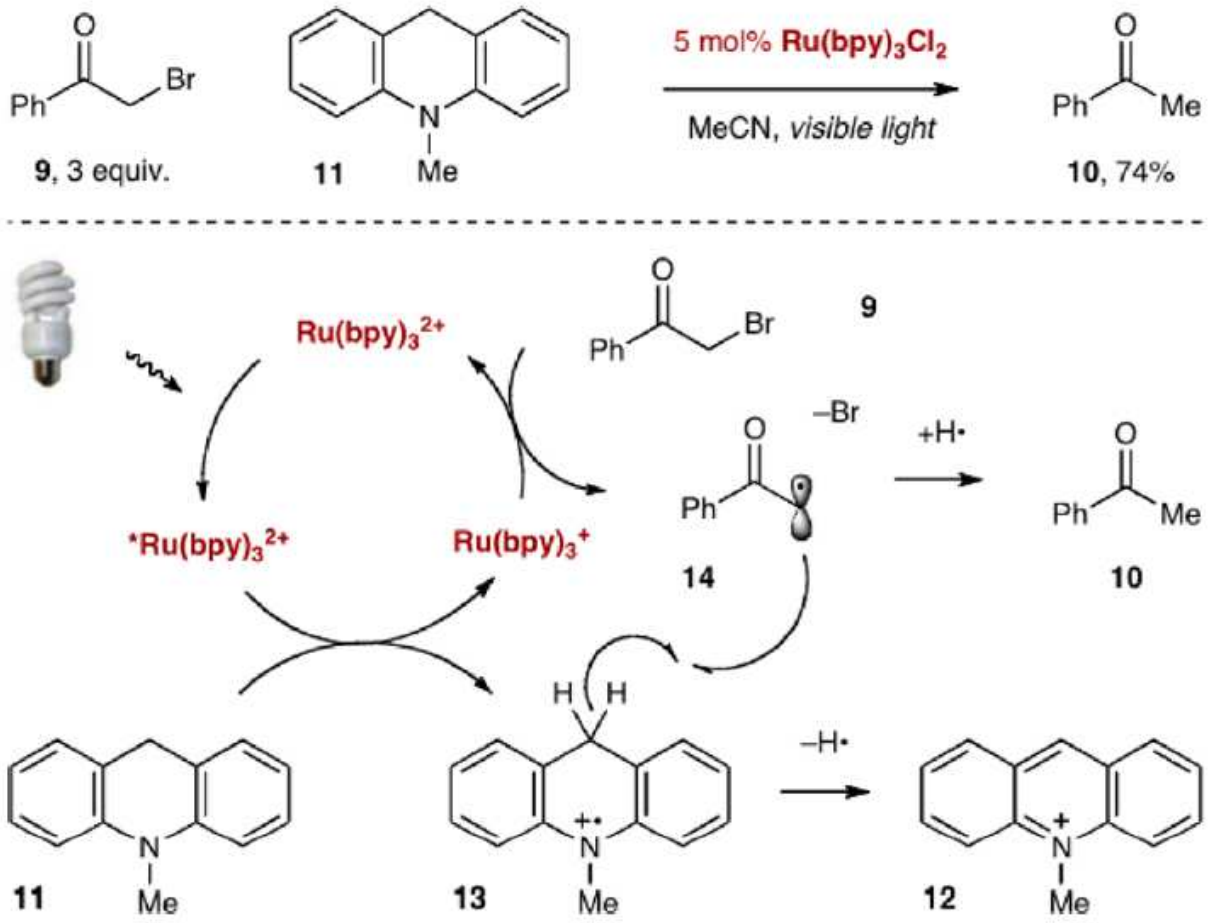
E: Anilinverbindung R_f = 0,04

N: Nitrosoverbindung R_f = 0,16

mit (N_{15} nach15 Minuten)

und (N_{45} nach 45 Minuten)


E
π*
π
π*
π
Grundzustand
Angeregter Zustand



Dihydroacridin

Prier, C.K.; Rankic, D.A.; MacMillan, D.W.C. *Chem. Rev.* **2013,** *113,* 5322-5363.