Oxidative and Reductive Carbodiazenylation of Nonactivated Olefins

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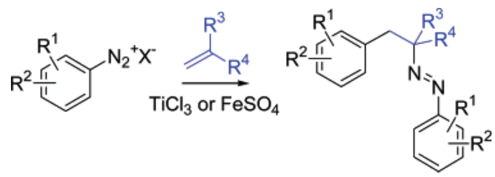


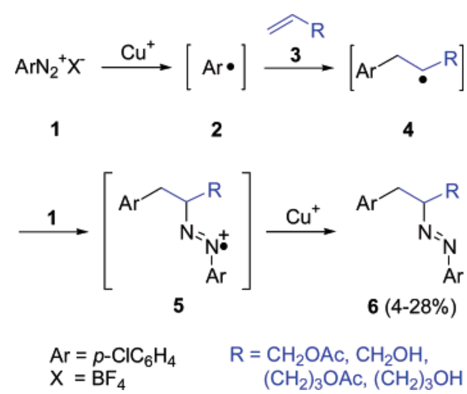
Procedures for the carbodiazenylation of nonactivated olefins with a wide range of aryldiazonium salts have been developed. The azo compounds obtained can serve as valuable precursors for β-arylamines (carboamination products), β-amino acids, ketones, and various heterocyclic structures.

Introduction

The carbodiazenylation of olefins was first observed by Levisalles and Rudler in 1976 during mechanistic studies of the Meerwein arylation (Scheme 1).[1,2] In the presence of copper(I) ions, the *p*-chlorophenyldiazonium salt **1** is reduced to give aryl radicals **2** after loss of nitrogen. Various monosubstituted, nonactivated olefins **3** were used to trap the highly reactive radical intermediates **2**. In the following step, the secondary radical **4** reacts with another aryldiazonium ion **1** to give radical cation **5**, which is finally reduced to azo compound **6**. The successful addition to the olefins **3** can be regarded as a proof for the radical character of the Meerwein reaction.

At this time, aryldiazonium ions were already well-known as potent electrophiles for azo couplings[3] and Japp–Klingemann[4] reactions. Though they had also been widely applied as sources for aryl radicals,[5] aryldiazonium ions had never before been described as nitrogen-centered radical scavengers. Similar observations and results were reported some years later by Citterio. Titanium(III) as a reducing agent gave the best results for the carbodiazenylation of 4-methyl-3-penten-2-one with *p*-chlorophenyldiazonium ions.[6] Though the reaction seemed to be limited to suitably substituted α,β-unsaturated olefins, it was

SCHEME 1. Carbodiazenylation Observed by Levisalles and Rudler



successfully applied for the synthesis of pyrazole derivatives.[7] Kinetic studies by Citterio showed that aryldiazonium salts are very efficient scavengers for nucleophilic tertiary radicals ($k = 10^8$ M^{-1} s^{-1} at 5 °C), whereas less nucleophilic primary alkyl radicals react significantly slower ($k = 10^6$ M^{-1} s^{-1}).[8] Attempts to achieve the carbodiazenylation of electron-rich olefins led in some cases to formation of aldehydes.[9] With ethyl vinyl ether and phenyldiazonium ions as reactants, the electron-transfer from

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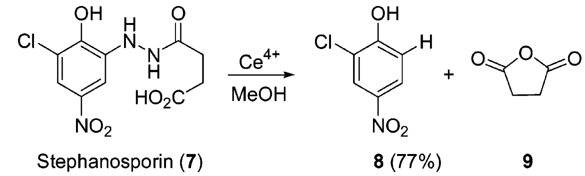
the radical intermediate **4** (Scheme 1, R = OEt) to give the corresponding cation is the preferred process over the diazo coupling reaction. In the case of the less electron-rich olefin vinyl acetate (Scheme 1, R = OAc), the expected carbodiazenylation product was observed in the reaction with phenyldiazonium ions, whereas *p*-cyanophenyldiazonium salts led again to the aldehyde. Small structural changes in both the diazonium salt and the olefin can therefore have a dramatic influence on the reaction pathway.[9] We were recently able to find suitable conditions for the reductive carbodiazenylation of nonactivated olefins with aryldiazonium salts.[10] An extension of the method toward aliphatic substituents via an intermediate iodine transfer has been reported as well as a diastereoselective approach via macrocyclization.[11] The synthesis of comparable azo compounds by ionic methods has been achieved by Baldwin via alkylations of azo anions[12] and thermal ene reactions.[13]

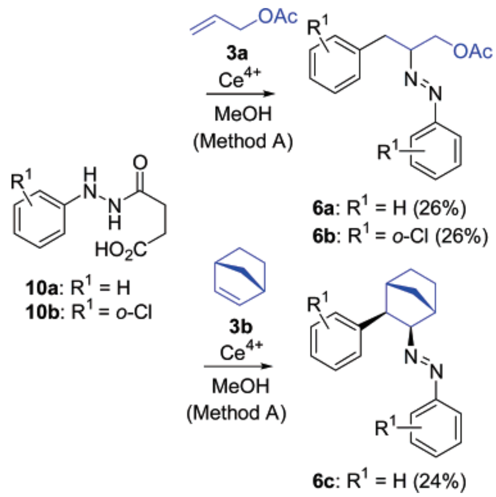
In recent years, sulfonyl azides have become the most well-known nitrogen-centered radical scavengers. The related carboazidation of olefins has been developed and intensively studied by Renaud.[14] Diastereoselective versions allowed an application for the synthesis of the natural product hyacinthacine A_1.[15] Next to sulfonyl azides and diazonium salts, radical additions to diazirines[16] and thionitrosyl compounds[17] have been described by Barton and Motherwell. Radical additions to azo dicarboxylates[18] have been reported by Cadogan.

Since the N−N double bond of azo compounds can be easily cleaved to the amine equivalents by hydrogenation, the carbodiazenylation reaction also represents the first part of an effective route to carboamination products. Several non-radical-based attempts have recently been made to achieve carboamination of nonactivated olefins and acetylenes. Among the organometallic methods, substituted pent-4-enylamines have been cyclized to give pyrrolidines via palladium catalysis.[19] 2-Alkynyl-substituted anilines[20] as well as isocyanates[21] have served as precursors for indoles in the presence of transition metals, and

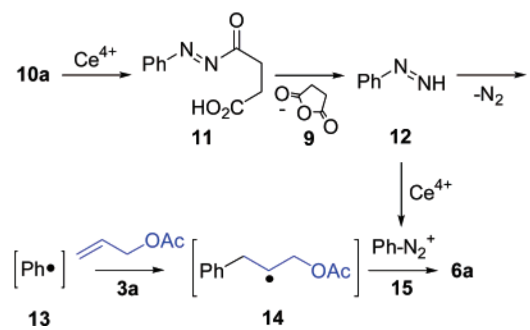
SCHEME 2. Oxidative Degradation of Stephanosporin



SCHEME 3. Oxidative Carbodiazenylation (Method A)



SCHEME 4. Oxidative Carbodiazenylation: Mechanism



imines have been reacted with alkynes using zirconium[22] and titanium[23] catalysts.

Results and Discussion

Oxidative Carbodiazenylation with Arylhydrazines. We first observed the carbodiazenylation of olefins in oxidative degradation experiments with substituted phenylhydrazines. The natural product stephanosporin (**7**), which was isolated from the carrot truffle *Stephanospora caroticolor*, was known to decompose, upon oxidation, to 2-chloro-4-nitrophenol (**8**) and succinic anhydride (**9**) via a mechanism that involves aryl radicals (Schemes 2 and 4).[24]

In one of our experiments, treatment of the simplified *N*-phenyl-*N′*-succinylhydrazine (**10a**)[25] with ceric ammonium nitrate (CAN) in a mixture of allyl acetate and methanol gave

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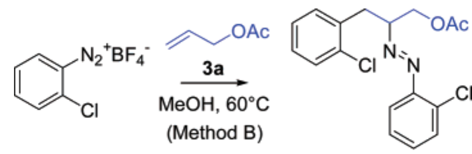
the carbodiazenylation product **6a** in 26% yield. The reaction was carried out at room temperature in degassed solvents under argon atmosphere. A strong evolution of nitrogen was observed immediately after the oxidant was added. The same yield of 26% was obtained with the 2-chloro derivative **10b**, which led to azo compound **6b**. When hydrazine **10a** was reacted with norbornene, the cis-substituted carbodiazenylation product **6c** (24%) was isolated.

Since several other 1-acyl-2-arylhydrazines are known to decompose via aryl radicals,[26] we tried to optimize the reaction by exchanging the succinyl group attached to the hydrazine **10a** for a phthaloyl or acetyl moiety. These experiments led to yields of **6a** in the range of only 10−20%. The use of unsubstituted phenylhydrazine gave 12% of **6a**. Reactions at temperatures other than room temperature, slow addition of ceric ammonium nitrate, as well as the use of other oxidants did not improve the result either.

The first part of the reaction mechanism shown in Scheme 4 is similar to the steps proposed for oxidative degradation of stephanosporin (**7**) (Scheme 2). Hydrazine **10a** is oxidized to diazene **11** which eliminates succinic anhydride (**9**) to give phenyldiazene (**12**).[27] The outcome of the oxidative carbodiazenylation is influenced mainly by two factors. First, diazene **12** has to serve as a source for phenyl radicals **13**[27] as well as for phenyldiazonium ions **15**. The diazonium ions **15** are needed for the trapping of intermediate **14**, but probably do not exist in high concentrations since they are continuously produced. Numerous oxidations of arylhydrazines to aryldiazonium salts via aryldiazenes are known in the literature and proceed with oxidants such as selenium dioxide,[28a] bromine or chlorine,[28b] nitric acid,[28c] copper(II),[28d] peroxides,[28e] and several others.[28f] We verified the presence of phenyldiazonium ions by an azo-coupling reaction.[29] When β-naphthol and sodium carbonate were added to the reaction mixture after the degradation of **10a** with CAN, the azo-coupling product 1-phenylazonaphthalen-2-ol[30] was isolated in 32% yield. The second problematic feature of the mechanism depicted in Scheme 4 is that a reductive step has to occur from **14** to product **6a** (see also Scheme 1, **5** → **6**) under oxidative conditions. The only potential reductant present in the reaction mixture seems to be the solvent methanol. Aliphatic alcohols like methanol and ethanol are among other solvents well-known for the dediazotization of aryl diazonium salts.[31,32] The temperature at which the process starts usually depends on the substituents attached to the aromatic ring of the diazonium salt. Since the alcohol-mediated dediazotization also proceeds via aryl radicals, the whole carbodiazenylation process should occur with methanol as the only reductant, given that methanol is able to reduce diazonium radical cations to azo compounds (Scheme 1, **5** → **6**).

SCHEME 5. Thermal Reductive Carbodiazenylation (Method B)



15a **6b** (45%)

Carbodiazenylation by Thermal Decomposition of Aryldiazonium Salts. To verify this hypothesis, *o*-chlorophenyldiazonium tetrafluoroborate (**15a**)[33] was dissolved in a degassed 1:1 mixture of allyl acetate and methanol. Stirring overnight at room temperature under argon led to low conversions, but up to 45% of carbodiazenylation product **6b** was isolated after 30 min when the solution was warmed to 60 °C (Scheme 4). Kinetic experiments showed that the presence of oxygen in the reaction mixture leads to delayed product formation.[31f]

As expected, heating under reflux led to a faster dediazotization of the diazonium salt **15a** ($t_{1/2}$ ∼ 10 min), but at this temperature (approximately 75 °C) the product **6b** also starts to suffer from significant degradation (Scheme 5). At 60 °C, the formation of side products from **6b** is sufficiently slow to allow moderate yields. Nevertheless, the process is troubled by polymerization and telomerization of allyl acetate.[34] These processes obviously start to occur toward the end of the reaction when the concentration of diazonium ions is too low for an effective trapping of the radical intermediates. As the oxidative and thermal reactions have already shown that the carbodiazenylation of nonactivated olefins can be achieved with higher yields than reported in the mechanistic studies of Levisalles and Rudler,[1] we turned toward an optimization of the reductant to allow a better controlled reaction at low temperatures.

Reductive Carbodiazenylation with Acceptor-Substituted Anilines. The reductants iron(II), titanium(III), and copper(I) as well as mixtures of these were used in test reactions for the carbodiazenylation. The results of the optimized process are summarized in Table 1. The best conditions that were found for the test reaction of methyl 4-aminobenzoate (**16d**) and allyl acetate (**3a**) (Table 1, entry 4) also gave good yields for all other aromatic amines **16** except for unsubstituted aniline (**16a**). In the latter case, a mixture of titanium(III) and iron (II) (method D) had to be used instead of titanium(III) as single reductant

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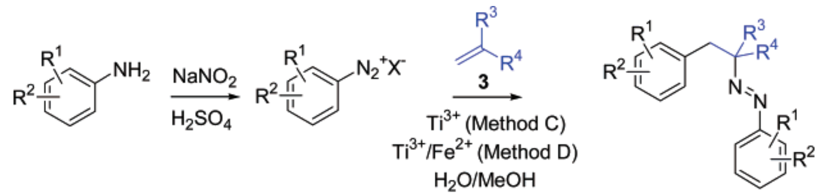
TABLE 1. Reductive Carbodiazenylation with Acceptor-Substituted Anilines (Methods C and D)



16 6

	aniline **16**			olefin **3**				
		R^1	R^2		R^3	R^4	product	yield[a] (%)
1	**16a**	H	H	**3a**	CH_2OAc	H	**6a**	47[c] (23)[b]
2	**16b**	*o*-Cl	H	**3a**	CH_2OAc	H	**6b**	67[b] (61)[c]
3	**16c**	*m*-Cl	*p*-CO_2H	**3a**	CH_2OAc	H	**6d**	55[c]
4	**16d**	*p*-CO_2Me	H	**3a**	CH_2OAc	H	**6e**	80[b]
5	**16e**	*o*-CO_2Me	H	**3a**	CH_2OAc	H	**6f**	59[b] (64)[d]
6	**16f**	*p*-CF_3	H	**3a**	CH_2OAc	H	**6g**	68[b]
7	**16d**	*p*-CO_2Me	H	**3c**	CH_2CN	H	**6h**	70[b]
8	**16d**	*p*-CO_2Me	H	**3d**	$(CH_2)_2COMe$	H	**6i**	60[b]
9	**16d**	*p*-CO_2Me	H	**3e**	CH_2OAc	Me	**6j**	58[b,e]
10	**16d**	*p*-CO_2Me	H	**3f**	CH_2OH	Me	**6k**	73[b,e]

[a] Isolated yield after column chromatography. [b] Method C (2.2 equiv of $TiCl_3$). [c] Method D (1.1 equiv of $TiCl_3$ + 4.0 equiv of $FeSO_4$). [d] Reaction on greater scale (5×). [e] Byproduct: 10−20% hydrazine.

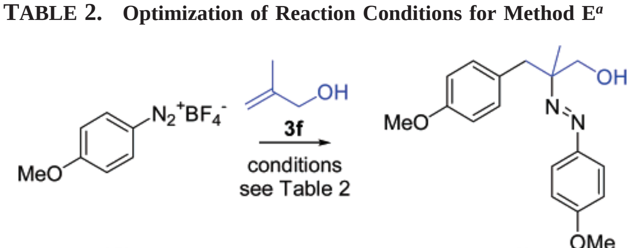
(method C). Both methods C and D are one-pot procedures that start from the aniline derivatives. Diazotation is achieved under standard conditions with sodium nitrite in 10% sulfuric acid at 0 °C. The subsequent addition of 20 vol % methanol to the reaction mixture enhanced the solubility of the olefins, while the finally formed products remained mostly insoluble. This insolubility protects the azo compounds from the acidic conditions of the reaction mixture. Isomerization to the hydrazones[10,35,36] and over-reduction to the hydrazines[10] by the excess of reductant therefore occur only to a very limited extent. The reactions (methods C and D) do not require dried or degassed solvents or a protective gas atmosphere. The removal of oxygen from the reaction mixture is secured by the reductant titanium(III).

The poor result which was obtained with method C and unsubstituted aniline **16a** already indicated that titanium(III) in combination with strong acidic conditions is probably not the best reductant for carbodiazenylations with electron-rich anilines or diazonium salts. Therefore, not surprisingly, an attempt with *p*-methoxyaniline and allyl acetate (**3a**) under the conditions of method C gave only 5% of the desired carbodiazenylation product.

Reductive Carbodiazenylation with Donor-Substituted Anilines. In order to close this open gap of substrates for carbodiazenylation, we tried to develop suitable conditions for the coupling of electron-rich aromatics to nonactivated double bonds. To avoid the strongly acidic conditions we chose to use the readily available and stable diazonium tetrafluoroborates as reactants. Selected results of the optimization are summarized in Table 2.

The first attempts with iron(II)sulfate heptahydrate in pure DMSO proceeded sluggishly, but when small amounts of water were added to the mixture, the reaction times (as indicated by nitrogen evolution) became notably shorter. A further increase of the aqueous part in the solvent mixture led to decreasing yields (Table 2, entries 1−3). Variation of the amount of iron(II) gave almost equal yields, as long its quantity did not fall below the stoichiometrically necessary amount of 1 equiv of iron(II) per diazonium salt (entries 1, 4, and 5). The observation that acceptable results can even be obtained with substoichiometric iron(II) supports the above assumption that the second reductive step (from the radical cation to the azo compound, Scheme 1, **5** → **6**) can also be accomplished by suitable solvents (entry 6). In this case, DMSO, like methanol before, seems to be acting as reductant for the azo radical cations. An experiment with a prolonged reaction time of 1 h showed that almost no

TABLE 2. Optimization of Reaction Conditions for Method E[a]



15b 6l

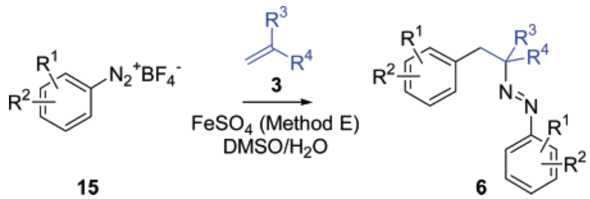
	reductant (equiv)[b]	reaction time (min)	solvents (mL)	yield[c] (%)
1	$FeSO_4$ (3)	15	DMSO (2) + H_2O (0.1)	62
2	$FeSO_4$ (3)	15	DMSO (2) + H_2O (0.5)	55
3	$FeSO_4$ (3)	15	DMSO (2) + H_2O (2)	11
4	$FeSO_4$ (1.5)	15	DMSO (2) + H_2O (1)	59
5	$FeSO_4$ (1.0)	15	DMSO (2) + H_2O (1)	58
6	$FeSO_4$ (0.5)	15	DMSO (2) + H_2O (1)	52
7	$FeSO_4$ (3)	60	DMSO (2) + H_2O (0.1)	59
8	$FeSO_4$ (3)	15	Acetone (2) + H_2O (1)	3
9	$FeSO_4$ (3)	15	DMF (2) + H_2O (1)	14
10	Cu_{powder} (3)	15	DMSO (2) + H_2O (1)	26
11	CuCl (3)	15	DMSO (2) + H_2O (1)	59

[a] All reactions were carried out with degassed solvents under argon atmosphere using 0.45 mmol of **15b** and 1.20 mmol of methallyl alcohol (**3f**). [b] Equivalents based on diazonium salt **15b**. [c] Yield determined by HPLC with methyl benzoate as internal standard.

(35) For studies on the isomerization of azo compounds and hydrazones, see: Kuznetsov, M. A.; Suvorov, A. A. *J. Org. Chem. USSR* **1982**, *18*, 1684−1691.

(36) We observed tautomerization of azo compound **6a** to the corresponding hydrazone in commercially available slightly acidic $CDCl_3$. NMR spectra of tautomerizable azo compounds were therefore measured in C_6D_6.

TABLE 3. Reductive Carbodiazenylation with Donor-Substituted Aryldiazonium Tetrafluoroborates (Method E)[a]



	aryldiazonium tetrafluoroborate 15			olefin 3			product 6	yield[b] (%)
		R^1	R^2		R^3	R^4		
1	**15b**	*p*-OMe	H	**3f**	CH_2OH	Me	**6l**	63
2	**15b**	*p*-OMe	H	**3a**	CH_2OAc	H	**6m**	58
3	**15b**	*p*-OMe	H	**3g**	$(CH_2)_2OH$	H	**6n**	56
4	**15b**	*p*-OMe	H	**3d**	$(CH_2)_2COMe$	H	**6o**	53
5	**15b**	*p*-OMe	H	**3e**	CH_2OAc	Me	**6p**	60
6	**15c**	*o*-OMe	*m*-OMe	**3f**	CH_2OH	Me	**6q**	52
7	**15d**	H	H	**3a**	CH_2OAc	H	**6a**	54
8	**15d**	H	H	**3h**	CH_2NHBoc	H	**6r**	48
9	**15e**	*o*-CO_2Me	H	**3a**	CH_2OAc	H	**6f**	52

[a] Method E (1.5 equiv of $FeSO_4$). [b] Isolated yield after column chromatography.

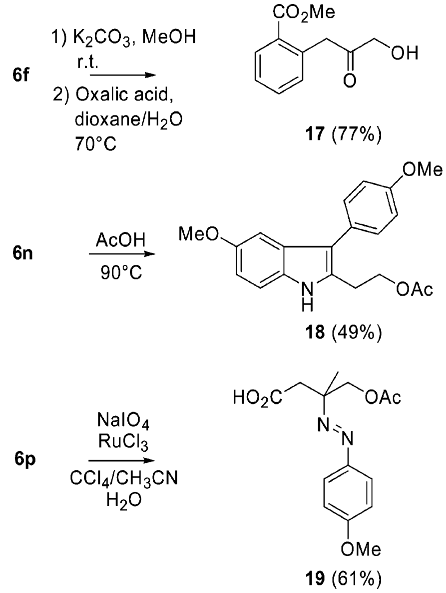
product degradation takes place under the reaction conditions (entries 1 and 7). In contrast to the acidic and aqueous methods C and D, where the azo products need to be protected from side reactions by their own insolubility, method E is mild enough to cause no product degradation in a nearly homogeneous mixture. A change of the solvents to acetone or DMF did not lead to an improvement (entries 8 and 9). Attempts with copper powder as reductant gave lower yields compared to copper(I) chloride, which was shown to be as effective as iron (II) (entries 10 and 11).

Since iron(II) salts gave the best results and are readily available at low cost, we chose iron(II) as reductant and DMSO as solvent for our further experiments. The results of the experiments that were carried out to explore the scope and limitations of method E are shown in Table 3.

We were pleased to find that donor- as well as acceptor-substituted aryldiazonium salts **15** gave the corresponding carbodiazenylation products **16** in synthetically useful yields. Only in the case of the electron-poor diazonium salt **15e** does the yield obtained with method E (Table 3, entry 9, 52%) appear to be slightly lower than the result of procedure C (Table 1, entry 5, 64%). On the other hand, 20−30 equiv of olefin was used in method C compared to 2.5 equiv for procedure E. The general advantages of method E over the procedures C and D are the lower amount of olefin, the applicability for electron-rich as well as for electron-poor aromatics, and the milder reaction conditions. As an example, the acid-labile Boc protecting group is well tolerated (Table 3, entry 8). Method E furthermore allows the carbodiazenylation of nonpolar olefins.[37] Methods C and D mainly benefit from the fact that they can be carried out as one-pot procedures without intermediate isolation of the diazonium salt. The reaction conditions are also less demanding since no degassed solvent is necessary. For all three methods C−E we often found an increase in yield when we were repeating the carbodiazenylation reactions on larger scales.

(37) For the effective carbodiazenylation of lipophilic olefins, the amount of water added to reaction mixture (method E) has to be reduced. This modification leads to prolonged reaction times of 1−2 h.

SCHEME 6. Further Synthetic Transformations of Carbodiazenylation Products



In general, the yields reported in Tables 1 and 3 are 5−10% higher when the reaction is carried out on a 5−10 times larger scale.

We have already reported the synthesis of a variety of heterocyclic structures which are directly accessible from the carbodiazenylation products.[10] The hydrogenation of the azo compounds to give the two carboamination products works best with Raney nickel. Three further examples to demonstrate the synthetic potential of the carbodiazenylation products are shown in Scheme 6. The first two transformations are based on the primary isomerization of the azo compounds to the corresponding aryl hydrazones. Only a few efficient procedures have been reported for the cleavage of hydrazones to ketones.[38,39] We obtained ketone **17** by isomerization of azo compound **6f** with potassium carbonate[10] in methanol and subsequent treatment with oxalic acid following a procedure reported by Baldwin.[13] In this way, ketone **17**[40] was obtained from **6f** in 77% yield. Heating of azo compounds **6e** and **6f** in a mixture of pyruvic acid, tetrahydrofuran, and water gave the desired products only in yields of up to 60%. Ketones such as **17** have recently been used as building blocks for natural product synthesis.[41]

Since α-aryl hydrazones can serve as substrates for Fischer indole synthesis, we warmed a solution of azo compound **6m** in acetic acid for 6 h to 90 °C. The desired indole **18** was isolated in 49% yield with the former hydroxy group of **6m** protected as an acetate.[42] The synthesis of electron-rich indoles such as **18** is often complicated by their instability toward strong acids,

(38) Hydrolytic cleavage of hydrazones to ketones: (a) Severin, T.; Poehlmann, H. *Chem. Ber.* **1978**, *111*, 1564−1577. (b) Kamal, A.; Rao, M. V.; Meshram, H. M. *Tetrahedron Lett.* **1991**, *32*, 2657−2658. (c) Nasreen, A.; Adapa, S. R. *Org. Prep. Proced. Int.* **1999**, *31*, 573−576. (d) Attanasi, O.; Gasperoni, S.; Carletti, C. *J. Prakt. Chem.* **1980**, *322*, 1063−1066. (e) De, S. K. *Synth. Commun.* **2004**, *34*, 4409−4416.

(39) Oxidative cleavage of hydrazones: (a) Barton, D. H. R.; Jaszberenyi, J. C.; Shinada, T. *Tetrahedron Lett.* **1993**, *34*, 7191−7194. (b) Barton, D. H. R.; Jaszberenyi, J. C.; Liu, W.; Shinada, T. *Tetrahedron* **1996**, *52*, 14673−14688.

(40) Bhakta, C. *J. Ind. Chem. Soc.* **1985**, *62*, 380−382.

(41) Chevenier, E.; Lucatelli, C.; Lucatelli, U.; Wang, W.; Gimbert, Y.; Greene, A. E. *Synlett* **2004**, 2693−2696.

(42) Strohmeier, J.; v. Angerer, E. *Arch. Pharm.* **1985**, *318*, 421−431.

which are generally used for indole cyclizations. Attempts to obtain indoles from **6m** with hydrochloric acid or trifluoroacetic acid at lower temperatures failed due to the instability of the product under stronger acidic conditions. Experiments with PCl_3,[43] which has been reported to be an effective reagent for indole cyclizations gave the desired heterocycles in lower yields.

The oxidation of *p*-methoxybenzyl derivatives to carboxylic acids was first reported by Sharpless.[44] Treatment of azo compound **6p** under similar conditions[45] gave the carboxylic acid **19** in 61% yield,[46] which shows that azo-substituted *p*-methoxyarenes are sufficiently stable under the oxidative conditions. The combination of carbodiazenylation and ruthenium periodate oxidation is therefore also a new strategy toward β-amino acid derivatives.

In summary, we have reported three titanium- and iron-based procedures (Methods C−E) for the reductive carbodiazenylation of nonactivated olefins. Donor- as well as acceptor-substituted anilines or aryldiazonium salts can now be used for the functionalization. The azo compounds that are obtained can serve as valuable precursors for numerous further transformations. The combination of the carbodiazenylation reaction with known methods opens new pathways for a quick and efficient access to β-arylamines, β-amino acids, ketones, and various heterocyclic structures including indoles. Almost all of the described compound types, especially the β-arylamines, have found numerous applications in medicinal chemistry. The carbodiazenylation methodology can therefore certainly facilitate the synthesis of new biologically active target molecules.

Experimental Section

Procedure for the Oxidative Carbodiazenylation (Method A). To solution of hydrazine **10** (2.0 mmol) in a degassed mixture of olefin (40 mmol) and MeOH (5 mL) was added solid ceric(IV)-ammonium nitrate (CAN) (3.3 g, 6.0 mmol) in one batch. The resulting mixture was stirred for 3 min at rt, diluted with water (50 mL), and extracted twice with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were washed with water and brine and dried over sodium sulfate.

Procedure for the Thermal Reductive Carbodiazenylation (Method B). To a degassed mixture of allyl acetate (4 mL) and MeOH (4 mL) was added diazonium tetrafluoroborate **15a** (168 mg, 0.74 mmol). The resulting mixture was warmed to 60 °C for 30 min, diluted with water, and extracted twice with Et_2O (2 × 50 mL). The combined organic extracts were washed with water and brine and dried over sodium sulfate. Purification by column chromatography gave azo compound **6b** (58 mg, 0.17 mmol, 45%) as a yellow oil.

Procedure for the Titanium(III)-Mediated Reductive Carbodiazenylation (Method C). To a solution of the aniline derivative (2.00 mmol) in 10% sulfuric acid (2.5 mL) at 0 °C was added dropwise a precooled solution of sodium nitrite (145 mg, 2.10 mmol) in water (0.5 mL). A precooled mixture of olefin (4.0 mL) and MeOH (1.0 mL) was added, and the resulting suspension was then treated dropwise with titanium(III) chloride (3.7 mL, 1.17 M aqueous solution, 4.40 mmol) over 15 min. The reaction mixture was stirred for additional 5 min at 0 °C. After the addition of water (50 mL), the aqueous phase was extracted three times with EtOAc or EtO_2 (3 × 50 mL, solvent depending on the polarity of the product). The combined organic phases were washed with water and brine and dried over sodium sulfate.

Procedure for the Titanium(III)/Iron(II)-Mediated Reductive Carbodiazenylation (Method D). To a solution of the aniline derivative (2.00 mmol) in 10% sulfuric acid (2.5 mL) at 0 °C was added dropwise a precooled solution of sodium nitrite (145 mg, 2.10 mmol) in water (0.5 mL). A precooled mixture of olefin (4.0 mL), MeOH (4.0 mL), and $FeSO_4 \cdot 2H_2O$ (1.50 g, 8.00 mmol) was added, and the resulting suspension was then treated dropwise with titanium(III) chloride (1.85 mL, 1.17 M aqueous solution, 2.20 mmol) over 15 min. The reaction mixture was stirred for an additional 15 min at 0 °C. After the addition of water (50 mL), the aqueous phase was extracted three times with EtOAc or Et_2O (3 × 50 mL, solvent depending on the polarity of the product). The combined organic phases were washed with water and brine and dried over sodium sulfate.

Aryldiazonium tetrafluoroborates were prepared by diazotation of corresponding anilines with sodium nitrite in 48% HBF_4 according to literature procedures.[31f]

Procedure for the Iron(II)-Mediated Reductive Carbodiazenylation (Method E). To a degassed solution of diazonium tetrafluoroborate **15** (2.25 mmol) in DMSO (5 mL) were added olefin **3** (6.00 mmol), $FeSO_4 \cdot 7H_2O$ (940 mg, 3.38 mmol), and water (1 mL) under argon atmosphere. After being stirred for 15 min at rt, the mixture was diluted with water (50 mL) and extracted with EtOAc or Et_2O (2 × 50 mL, solvent depending on the polarity of the product). The combined organic phases were washed with water and brine and dried over sodium sulfate.

Acetic Acid 3-Phenyl-2-phenylazopropyl Ester (6a) (Methods A, D, and E). Purification by column chromatography (100% P → P/EtOAc = 10:1) gave **6a** as a yellow oil: $R_f = 0.20$ (P/EtOAc = 20:1); ^1H NMR (C_6D_6, 360 MHz) δ = 1.55 (s, 3 H), 2.91 (dd, $^3J = 6.8$ Hz, $^2J = 13.7$ Hz, 1 H), 3.06 (dd, $^3J = 7.6$ Hz, $^2J = 13.7$ Hz, 1 H), 4.35 (m, 1 H), 4.42 (dd, $^3J = 3.8$ Hz, $^2J = 11.3$ Hz, 1 H), 4.65 (dd, $^3J = 8.1$ Hz, $^2J = 11.3$ Hz, 1 H), 6.98−7.20 (m, 8 H), 7.77 (m, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ = 20.2 (CH_3), 36.9 (CH_2), 64.8 (CH_2), 77.4 (CH), 122.8 (2 × CH), 126.7 (CH), 128.7 (2 × CH), 129.2 (2 × CH), 129.8 (2 × CH), 130.8 (CH), 137.7 (C_q), 152.5 (C_q), 169.9 (C_q); MS (EI) *m/z* 282 (1) [M^+], 222 (2), 177 (10), 117 (26), 105 (92), 77 (100); HRMS (EI) calcd for $C_{17}H_{18}N_2O_2$ [M^+] 282.1380, found 282.1368.

Acetic Acid 3-(2-Chlorophenyl)-2-(2-chlorophenylazo)propyl Ester (6b) (Methods A, B, C, and D). Purification by column chromatography (100% P → P/EtOAc = 10:1) gave **6b** as a yellow oil: $R_f = 0.20$ (P/EtOAc = 20:1); ^1H NMR (C_6D_6, 360 MHz) δ 1.60 (s, 3 H), 3.12 (dd, $^3J = 5.9$ Hz, $^2J = 14.0$ Hz, 1 H), 3.26 (dd, $^3J = 7.6$ Hz, $^2J = 14.0$ Hz, 1 H), 4.43 (dd,$^3J = 3.2$ Hz, $^2J = 11.0$ Hz, 1 H), 4.51−4.59 (m, 1 H), 4.63 (dd, $^3J = 7.7$ Hz, $^2J = 11.0$ Hz, 1 H), 6.69−6.80 (m, 4 H), 6.88 (dd, $^4J = 1.8$ Hz, $^3J = 7.6$ Hz, 1 H), 7.08−7.14 (m, 2 H), 7.36 (dd, $^4J = 1.6$ Hz, $^3J = 7.7$ Hz, 1 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 20.2 (CH_3), 34.0 (CH_2), 64.4 (CH_2), 76.2 (CH), 118.3 (CH), 126.9 (CH), 127.3 (CH), 128.2 (CH), 129.9 (CH), 130.6 (CH), 131.5 (CH), 131.9 (CH), 134.3 (C_q), 134.7 (C_q), 135.5 (C_q), 148.7 (C_q), 169.9 (C_q); MS (EI) *m/z* 350 (<1) [M^+, $C_{17}H_{16}{}^{35}Cl_2N_2O_2$], 210 (4), 169 (7), 167 (20), 141 (4), 139 (10), 127 (34), 125 (100), 111 (6); HRMS (EI) calcd for $C_{17}H_{16}{}^{35}Cl_2N_2O_2$ [M^+] 350.0589, found 305.0603.

(1*R*,2*S*,3*S*,4*S*)- and (1*S*,2*R*,3*R*,4*R*)-Phenyl(3-phenylbicyclo-[2.2.1]hept-2-yl)diazene (6c) (Method A). Purification by column chromatography (100% P → P/EtOAc = 10:1) gave **6c** as a yellow oil: $R_f = 0.45$ (P/EtOAc = 20:1); ^1H NMR (C_6D_6, 600 MHz) δ 1.16−1.20 (m, 2 H), 1.36 (d, $^2J = 9.6$ Hz, 1 H), 1.47−1.50 (m, 2 H), 2.33 (s, 1 H), 2.64 (s, 1 H), 2.79 (d, $^2J = 9.6$ Hz, 1 H), 2.99 (d, $^3J = 7.8$ Hz, 1 H), 4.12 (d, $^3J = 7.8$ Hz, 1 H), 6.90−6.95 (m, 2 H), 7.00 (t, $^3J = 7.8$ Hz, 2 H), 7.04 (t, $^3J = 7.5$ Hz, 2 H), 7.10 (d, ^3J

(43) Baccolini, G.; Dalpozzo, R.; Todesco, P. E. *J. Chem. Soc., Perkin Trans. 1* **1988**, 971−974.
(44) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, B. *J. Org. Chem.* **1981**, *46*, 3936−3938.
(45) Kim, B. J.; Park, Y. S.; Beak, P. *J. Org. Chem.* **1999**, *64*, 1705−1708.
(46) Yield based on recovered starting material. Though additional $RuCl_3$ was added to the reaction mixture, no complete conversion was observed. An experiment over 24 h without further addition of $RuCl_3$ gave 41% of **19** and 42% of recovered **6p** (65% yield based on recovered starting material).

= 7.5 Hz, 2 H), 7.27 (d, ^3J = 7.8 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ = 26.3 (CH_2), 31.2 (CH_2), 36.2 (CH_2), 41.3 (CH), 43.7 (CH), 53.9 (CH), 84.7 (CH), 122.4 (2 × CH), 125.6 (CH), 128.1 (2 × CH), 128.8 (2 × CH), 129.0 (2 × CH), 129.8 (CH), 141.2 (C_q), 153.1 (C_q); MS (EI) *m/z* 276 (27) [M^+], 171 (55), 105 (37), 91 (100), 77 (48); HRMS (EI) calcd for $C_{19}H_{20}N_2$ [M^+] 276.1627, found 276.1623.

Acetic Acid 3-(4-Carboxy-3-chlorophenyl)-2-(4-carboxy-3-chlorophenylazo)propyl Ester (6d). Purification by column chromatography ($CHCl_3$/MeOH = 7:3) gave **6d** as a yellow foam: R_f = 0.70 ($CHCl_3$/MeOH = 2:1); ^{1}H NMR (CD_3OD, 360 MHz) δ 1.97 (s, 3 H), 3.19 (dd, ^3J = 5.5 Hz, ^2J = 14.0 Hz, 1 H), 3.28 (dd, ^3J = 8.5 Hz, ^2J = 14.0 Hz, 1 H), 4.20−4.25 (m, 1 H), 4.49 (dd, ^3J = 3.5 Hz, ^2J = 11.5 Hz, 1 H) 4.59 (dd, ^3J = 8.0 Hz, ^2J = 11.5 Hz, 1 H), 7.11 (dd, ^4J = 1.8 Hz, ^3J = 7.9 Hz, 1 H), 7.24 (d, ^4J = 1.8 Hz, 1 H), 7.51 (d, ^3J = 7.9 Hz, 1 H), 7.55 (dd, ^3J = 1.8 Hz, ^2J = 7.9 Hz, 1 H), 7.58 (d, ^4J = 1.8 Hz, 1 H), 7.63 (d, ^3J = 7.9 Hz, 1 H); ^{13}CNMR (CD_3OD, 90 MHz) δ 20.6 (CH_3), 36.6 (CH_2), 65.6 (CH_2), 78.2 (CH), 122.3 (CH), 123.9 (CH), 128.9 (CH), 130.5 (CH), 130.7 (CH), 132.2 (CH), 132.4 (C_q), 132.5 (C_q), 136.7 (C_q), 141.6 (C_q), 142.3 (C_q), 153.2 (C_q), 171.9 (C_q), 172.4 (2 × C_q); MS (ESI) *m/z* 437 [M^+ − H, $C_{19}H_{15}{}^{35}Cl_2N_2O_6$], 439 [$M^+$ − H, $C_{19}H_{15}{}^{35}Cl^{37}$-$ClN_2O_6$]; HRMS (ESI) calcd for $C_{19}H_{16}{}^{35}Cl_2N_2O_6$ [M^+] 437.0307, found 437.0299.

4-[3-Acetoxy-2-(4-methoxycarbonylphenylazo)propyl]benzoic Acid Methyl Ester (6e). Purification by column chromatography (P/EtOAc = 3:1) gave **6e** as a yellow solid: R_f = 0.60 (P/EtOAc = 2:1); mp = 88 °C; ^{1}H NMR (C_6D_6, 360 MHz) δ 1.60 (s, 3 H), 2.83 (dd, ^3J = 6.3 Hz, ^2J = 13.9 Hz, 1 H), 3.00 (dd, ^3J = 7.9 Hz, ^2J = 13.9 Hz, 1 H), 3.48 (s, 3 H), 3.51 (s, 3 H), 4.20−4.28 (m, 1 H), 4.39 (dd, ^3J = 3.6 Hz, ^2J = 11.5 Hz, 1 H) 4.56 (dd, ^3J = 7.9 Hz, ^2J = 11.5 Hz, 1 H), 6.92 (d, ^3J = 8.3 Hz, 2 H), 7.63 (d, ^3J = 8.6 Hz, 2 H), 8.01 (d, ^3J = 8.3 Hz, 2 H), 8.07 (d, ^3J = 8.6 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 20.2 (CH_3), 36.5 (CH_2), 51.5 (CH_3), 51.8 (CH_3), 64.5 (CH_2), 77.3 (CH), 122.5 (2 × CH), 129.3 (C_q), 129.8 (2 × CH), 130.1 (2 × CH), 130.9 (2 × CH), 132.6 (C_q), 142.7 (C_q), 154.5 (C_q), 165.9 (C_q), 166.4 (C_q), 169.8 (C_q); MS (EI) *m/z* 398 (6) [M^+], 367 (5), 279 (5), 235 (10), 163 (72), 136 (10), 135 (100), 102 (10); HRMS (EI) calcd for $C_{21}H_{22}N_2O_6$ [M^+] 398.1478, found 398.1472.

2-[3-Acetoxy-2-(2-methoxycarbonylphenylazo)propyl]benzoic Acid Methyl Ester (6f). Purification by column chromatography (P/EtOAc = 3:1) gave **6f** as a yellow oil: R_f = 0.25 (P/EtOAc = 4:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.69 (s, 3 H), 3.46 (s, 3 H), 3.48 (s, 3 H), 3.60 (dd, ^3J = 7.9 Hz, ^2J = 13.5 Hz, 1 H), 3.71 (dd, ^3J = 5.8 Hz, ^2J = 13.5 Hz, 1 H), 4.56 (dd, ^3J = 3.8 Hz, ^2J = 11.1 Hz, 1 H) 4.58−4.65 (m, 1 H), 4.78 (dd, ^3J = 7.6 Hz, ^2J = 11.1 Hz, 1 H), 6.87−6.93 (m, 2 H), 6.95−7.04 (m, 3 H), 7.23 (dd, ^4J = 1.1 Hz, ^3J = 7.9 Hz, 1 H), 7.61 (dd, ^4J = 1.3 Hz, ^3J = 7.7 Hz, 1 H), 7.88 (d, ^3J = 7.9 Hz, 1 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 20.4 (CH_3), 35.0 (CH_2), 51.5 (CH_3), 51.8 (CH_3), 64.8 (CH_2), 77.6 (CH), 119.2 (CH), 126.8 (CH), 128.8 (C_q), 129.3 (CH), 129.8 (CH), 130.4 (C_q), 131.4 (CH), 131.8 (CH), 132.0 (CH), 132.7 (CH), 140.1 (C_q), 152.1 (C_q), 167.2 (C_q), 167.5 (C_q), 170.0 (C_q); MS (EI) *m/z* 398 (8) [M^+], 279 (6), 235 (22), 163 (65), 135 (100), 115 (8), 91 (12); HRMS (EI) calcd for $C_{21}H_{22}N_2O_6$ [M^+] 398.1478, found 398.1472.

Acetic Acid 3-(4-Trifluoromethyl-phenyl)-2-(4-trifluoromethylphenylazo)propyl Ester (6g). Purification by column chromatography (P/EtOAc = 10:1) gave **6g** as a yellow solid: R_f = 0.25 (P/EtOAc = 10:1); mp = 79 °C; ^{1}H NMR (C_6D_6, 360 MHz) δ 1.63 (s, 3 H), 2.78 (dd, ^3J = 2.5 Hz, ^2J = 13.7 Hz, 1 H), 2.95 (dd, ^3J = 7.9 Hz, ^2J = 13.7 Hz, 1 H), 4.14−4.23 (m, 1 H), 4.33 (dd, ^3J = 4.0 Hz, ^2J = 11.5 Hz, 1 H) 4.49 (dd, ^3J = 7.9 Hz,^2J = 11.5 Hz, 1 H), 6.82 (d, ^3J = 7.9 Hz, 2 H), 7.27 (d, ^3J = 7.9 Hz, 2 H), 7.31 (d, ^3J = 7.9 Hz, 2 H), 7.48 (d, ^3J = 7.9 Hz, 2 H); ^{13}CNMR (C_6D_6, 90 MHz) δ 20.0 (CH_3), 36.1 (CH_2), 64.2 (CH_2), 77.0 (CH), 122.8 (2×CH), 124.4 (q, $^1J_{CF}$ = 273.0 Hz, C_q), 124.9 (q, $^1J_{CF}$ = 272.1 Hz, C_q) 125.6 (q, $^3J_{CF}$ = 3.8 Hz, 2 × CH), 126.5 (q, $^3J_{CF}$ = 3.9 Hz, 2 × CH), 129.2 (q, $^2J_{CF}$ = 32.2 Hz, C_q), 130.0 (2 × CH), 132.5 (q, $^2J_{CF}$ = 32.3 Hz, C_q), 141.7 (C_q), 153.8 (C_q), 169.8 (C_q); ^{19}F NMR (C_6D_6, 235 MHz) δ −62.2 (CF_3), −62.5 (CF_3); MS (EI) *m/z* 418 (3) [M^+], 399 (3), 339 (4) 328 (6), 305 (8), 245 (18), 201 (8), 185 (14), 173 (62), 159 (59), 145 (100); HRMS (EI) calcd for $C_{19}H_{16}F_6N_2O_2$ [M^+] 418.1116, found 418.1117.

4-[2-(4-Methoxycarbonylphenylazo)-3-cyanopropyl]benzoic Acid Methyl Ester (6h). Purification by column chromatography (P/EtOAc = 3:1) gave **6h** as a yellow solid: R_f = 0.25 (P/EtOAc = 3:1); mp = 74 °C; ^{1}H NMR (C_6D_6, 360 MHz) δ 2.13 (dd, ^3J = 5.0 Hz, ^2J = 16.6 Hz, 1 H), 2.19 (dd, ^3J = 5.9 Hz, ^2J = 16.6 Hz, 1 H), 2.84 (dd, ^3J = 6.8 Hz, ^2J = 14.0 Hz, 1 H), 2.99 (dd, ^3J = 7.2 Hz, ^2J = 14.0 Hz, 1 H), 3.54 (s, 3 H), 3.56 (s, 3 H), 3.93−4.02 (m, 1 H), 6.93 (d, ^3J = 8.2 Hz, 2 H), 7.61 (d, ^3J = 8.2 Hz, 2 H), 7.99 (d, ^3J = 8.2 Hz, 2 H), 8.06 (d, ^3J = 8.2 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 20.1 (CH_2), 38.4 (CH_2), 51.5 (CH_3), 51.8 (CH_3), 73.0 (CH), 117.0 (C_q), 122.6 (2 × CH), 129.5 (C_q), 129.8 (2 × CH), 130.2 (2 × CH), 130.9 (2 × CH), 132.9 (C_q), 141.9 (C_q), 154.0 (C_q), 165.9 (C_q), 166.4 (C_q); MS (EI) *m/z* 365 (11) [M^+], 334 (8), 242 (4), 211 (5), 188 (5), 163 (76), 151 (12), 149 (16), 136 (12), 135 (100), 120 (16), 103 (15); HRMS (EI) calcd for $C_{20}H_{19}N_3O_4$ [M^+] 365.1375, found 365.1370.

4-[2-(4-Methoxycarbonylphenylazo)-5-oxohexyl]benzoic Acid Methyl Ester (6i). Purification by column chromatography (P/EtOAc = 3:1) gave **6i** as a yellow oil: R_f = 0.30 (P/EtOAc = 3:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.60 (s, 3 H), 1.93−2.05 (m, 3 H), 2.11−2.20 (m, 1 H), 2.84 (dd, ^3J = 5.6 Hz, ^2J = 13.8 Hz, 1 H), 3.08 (dd, ^3J = 7.9 Hz, ^2J = 13.8 Hz, 1 H), 3.48 (s, 3 H), 3.49 (s, 3 H), 3.86−3.92 (m, 1 H), 6.97 (d, ^3J = 8.3 Hz, 2 H), 7.60 (d, ^3J = 9.0 Hz, 2 H), 7.98 (d, ^3J = 8.3 Hz, 2 H), 8.06 (d, ^3J = 9.0 Hz, 2 H); ^{13}C NMR (C_6D_6, 90.6 MHz) δ 27.4 (CH_2), 29.4 (CH_3), 39.6 (CH_2), 40.3 (CH_2), 51.5 (CH_3), 51.8 (CH_3), 78.4 (CH), 122.4 (2 × CH), 129.0 (C_q), 129.9 (2 × CH), 130.0 (2 × CH), 130.9 (2 × CH), 132.4 (C_q), 143.9 (C_q), 154.5 (C_q), 166.0 (C_q), 166.5 (C_q), 205.6 (C_q); MS (EI) *m/z* 396 (2) [M^+], 365 (10), 234 (11), 233 (71), 201 (68), 175 (12), 163 (34), 149 (20), 135 (100), 120 (25); HRMS (EI) calcd for $C_{22}H_{24}N_2O_5$ [M^+] 396.1685, found 396.1706; HRMS (EI) calcd for $C_{21}H_{21}N_2O_4$ [M^+ − CH_3O] 365.1501, found 365.1498.

4-[3-Acetoxy-2-methyl-2-(4-methoxycarbonylphenylazo)propyl]benzoic Acid Methyl Ester (6j). Purification by column chromatography (P/EtOAc = 4:1) gave **6j** as a yellow oil: R_f = 0.60 (P/EtOAc = 4:1); ^{1}H NMR (C_6D_6, 250 MHz) δ 1.14 (s, 3 H), 1.64 (s, 3 H), 2.94 (d, ^2J = 13.3 Hz, 1 H), 3.06 (d, ^2J = 13.3 Hz, 1 H), 3.49 (s, 3 H), 3.50 (s, 3 H), 4.41 (s, 2 H), 6.95 (d, ^3J = 8.3 Hz, 2 H), 7.61 (d, ^3J = 8.8 Hz, 2 H), 7.97 (d, ^3J = 8.3 Hz, 2 H), 8.09 (d, ^3J = 8.8 Hz, 2 H); ^{13}C NMR (C_6D_6, 63 MHz) δ 19.6 (CH_3), 20.3 (CH_3), 42.1 (CH_2), 51.6 (CH_3), 51.8 (CH_3), 67.9 (CH_2), 73.3 (C_q), 122.4 (2 × CH), 129.3 (C_q), 129.7 (2 × CH), 130.9 (2 × CH), 131.0 (2 × CH), 132.4 (C_q), 142.1 (C_q), 154.4 (C_q), 165.9 (C_q), 166.5 (C_q), 169.8 (C_q); MS (EI) *m/z* 382 (2) [M^+ − CH_2O], 381 (8) [M^+ − CH_3O], 249 (34), 217 (23), 207 (34), 189 (26), 175 (25), 163 (53), 149 (34), 135 (100); HRMS (EI) calcd for $C_{22}H_{24}N_2O_6$ [M^+] 412.1634, found 412.1626; HRMS (EI) calcd for $C_{21}H_{21}N_2O_5$ [M^+ − CH_3O] 381.1450, found 381.1445.

4-[3-Hydroxy-2-methyl-2-(4-methoxycarbonylphenylazo)propyl]benzoic Acid Methyl Ester (6k). Purification by column chromatography (P/EtOAc = 2:1) gave **6k** as a yellow oil: R_f = 0.50 (P/EtOAc = 2:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.10 (s, 3 H), 2.97 (d, ^2J = 13.0 Hz, 1 H), 3.07 (d, ^2J = 13.0 Hz, 1 H), 3.48 (s, 3 H), 3.49 (s, 3 H), 3.62 (d, ^2J = 11.5 Hz, 1 H), 3.69 (d, ^2J = 11.5 Hz, 1 H), 7.10 (d, ^3J = 8.3 Hz, 2 H), 7.54 (d, ^3J = 8.6 Hz, 2 H), 8.03 (d, ^3J = 8.3 Hz, 2 H), 8.10 (d, ^3J = 8.6 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 19.6 (CH_3), 41.5 (CH_2), 51.6 (CH_3), 51.8 (CH_3), 66.9 (CH_2), 75.2 (C_q), 122.4 (2 × CH), 129.2 (C_q), 129.7 (2 × CH), 130.9 (2 × CH), 131.2 (2 × CH), 132.4 (C_q), 142.9 (C_q), 154.4 (C_q), 166.0 (C_q), 166.7 (C_q); MS (EI) *m/z* 340 (34) [M^+ − CH_2O], 309 (13), 207 (36), 175 (28), 163 (25), 151 (34), 150 (23), 149 (100), 136 (15), 135 (58), 122 (15), 121 (28), 120 (18); HRMS

(EI) calcd for $C_{20}H_{22}N_2O_5$ [M^+] 370.1529, found 370.1510; HRMS (EI) calcd for $C_{19}H_{20}N_2O_4$ [$M^+ - CH_2O$] 340.1423, found 340.1421.

3-(4-Methoxyphenyl)-2-(4-methoxyphenylazo)-2-methylpropan-1-ol (6l). Purification by column chromatography (P/EtOAc = 4:1 → 2:1) gave **6l** as a yellow oil: R_f = 0.30 (P/EtOAc = 3:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.24 (s, 3 H), 2.97 (d, ^2J = 13.7 Hz, 1 H), 3.11 (d, ^2J = 13.7 Hz, 1 H), 3.74−3.79 (m, 2 H), 3.77 (s, 3 H), 3.84 (s, 3 H), 6.82 (d, ^3J = 8.6 Hz, 2 H), 6.97 (d, ^3J = 9.0 Hz, 2 H), 7.16 (d, ^3J = 8.6 Hz, 2 H), 7.71 (d,^3J = 9.0 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 19.5 (CH_3), 40.6 (CH_2), 54.9 (CH_3), 55.3 (CH_3), 66.9 (CH_2), 73.1 (C_q), 113.2 (2 × CH), 113.9 (2 × CH), 123.7 (2 × CH), 129.0 (C_q), 131.5 (2 × CH), 145.7 (C_q), 158.0 (C_q), 161.5 (C_q); MS (EI) *m*/*z* 314 (6) [M^+], 284 (5), 250 (5), 206 (7), 179 (26), 135 (46), 121 (100), 107 (47), 77 (12); HRMS (EI) calcd for $C_{18}H_{22}N_2O_3$ [M^+] 314.1631, found 314.1621.

Acetic Acid 3-(4-Methoxyphenyl)-2-(4-methoxyphenylazo)-propyl Ester (6m). Purification by column chromatography (P/EtOAc = 4:1) gave **6m** as a yellow oil: R_f = 0.60 (P/EtOAc = 3:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.57 (s, 3 H), 2.93 (dd, ^3J = 6.8 Hz, ^2J = 14.0 Hz, 1 H), 3.08 (dd, ^3J = 7.2 Hz, ^2J = 14.0 Hz, 1 H), 3.18 (s, 3 H), 3.26 (s, 3 H), 4.32−4.36 (m, 1 H), 4.48 (dd, ^3J = 3.8 Hz, ^2J = 11.2 Hz, 1 H), 4.71 (dd, ^3J = 8.3 Hz, ^2J = 11.2 Hz, 1 H), 6.68 (d, ^3J = 9.0 Hz, 2 H), 6.69 (d, ^3J = 9.0 Hz, 2 H), 6.96 (d, ^3J = 9.0 Hz, 2 H), 7.84 (d, ^3J = 9.0 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 20.3 (CH_3), 36.3 (CH_2), 54.7 (CH_3), 55.0 (CH_3), 65.1 (CH_2), 77.3 (CH), 114.2 (2 × CH), 114.3 (2 × CH), 124.7 (2 × CH), 129.6 (C_q), 130.8 (2 × CH), 146.7 (C_q), 158.8 (C_q), 161.2 (C_q), 170.0 (C_q); MS (EI) *m*/*z* 342 (4) [M^+], 207 (14), 147 (35), 135 (96), 121 (35), 108 (15), 107 (100), 92 (16), 91 (14), 77 (51); HRMS (ESI) calcd for $C_{19}H_{23}N_2O_4$ [$M^+ + H$] 343.1653, found 343.1643.

4-(4-Methoxyphenyl)-3-(4-methoxyphenylazo)butan-1-ol (6n). Purification by column chromatography (P/EtOAc = 2:1→1:1) gave **6n** as a yellow oil: R_f = 0.40 (P/EtOAc = 1:1); ^{1}H NMR (C_6D_6, 250 MHz) δ 1.93−2.04 (m, 1 H), 2.11−2.23 (m, 1H), 2.96 (dd, ^3J = 6.3 Hz, ^2J = 13.9 Hz, 1 H), 3.18 (dd,^3J = 7.6 Hz, ^2J = 13.9 Hz, 1 H), 3.21 (s, 3H), 3.28 (s, 3H), 3.48−3.59 (m, 2 H), 4.17−4.26 (m, 1 H), 6.68 (d, ^3J = 8.6 Hz, 2 H), 6.71 (d, ^3J = 8.6 Hz, 2 H), 7.01 (d, ^3J = 8.6 Hz, 2 H), 7.77 (d,^3J = 8.6 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 36.3 (CH_2), 39.8 (CH_2), 54.7 (CH_3), 55.0 (CH_3), 59.7 (CH_2), 76.2 (CH), 114.1 (2 × CH), 114.4 (2 × CH), 124.5 (2 × CH), 130.8 (C_q), 130.9 (2 × CH), 146.6 (C_q), 158.6 (C_q), 162.0 (C_q); MS (EI) *m*/*z* 314 (13) [M^+], 294 (8), 194 (10), 179 (32), 161 (25), 135 (97), 121 (73), 107 (100), 77 (21); HRMS (EI) calcd for $C_{18}H_{22}N_2O_3$ [M^+] 314.1631, found 314.1622.

6-(4-Methoxyphenyl)-5-(4-methoxyphenylazo)hexan-2-one (6o). Purification by column chromatography (P/EtOAc = 3:1) gave **6o** as a yellow oil: R_f = 0.30 (P/EtOAc = 4:1); ^{1}H NMR (C_6D_6, 500 MHz) δ 1.56 (s, 3 H), 1.95−2.15 (m, 3 H), 2.22−2.32 (m, 1 H), 2.93 (dd, ^3J = 6.3 Hz, ^2J = 13.8 Hz, 1 H), 3.15 (dd, ^3J = 7.3 Hz, ^2J = 13.8 Hz, 1 H), 3.25 (s, 3 H), 3.29 (s, 3 H), 3.86−3.94 (m, 1 H), 6.70 (d, ^3J = 8.5 Hz, 2 H), 6.73 (d, ^3J = 8.5 Hz, 2 H), 7.01 (d, ^3J = 8.5 Hz, 2 H), 7.80 (d, ^3J = 9.0 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 27.4 (CH_2), 29.4 (CH_3), 39.9 (CH_2), 40.0 (CH_2), 54.7 (CH_3), 55.0 (CH_3), 78.4 (CH), 114.1 (2 × CH), 114.4 (2 × CH), 124.5 (2 × CH), 130.7 (C_q), 130.9 (2 × CH), 146.6 (C_q), 158.7 (C_q), 162.0 (C_q), 205.9 (C_q); MS (EI) *m*/*z* 340 (14) [M^+], 205 (47), 147 (68), 135 (98), 121 (22), 107 (100), 92 (6), 91 (6), 77 (16); HRMS (EI) calcd for $C_{20}H_{24}N_2O_3$ [M^+] 340.1787, found 340.1787.

Acetic Acid 3-(4-Methoxyphenyl)-2-(4-methoxyphenylazo)-2-methylpropyl Ester (6p). Purification by column chromatography (P/EtOAc = 4:1) gave **6p** as a yellow oil: R_f = 0.45 (P/EtOAc = 4:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.30 (s, 3 H), 1.66 (s, 3 H), 3.06 (d, ^2J = 13.7 Hz, 1 H), 3.13 (d, ^2J = 13.7 Hz, 1 H), 3.24 (s, 3 H), 3.29 (s, 3 H), 4.51 (d, ^2J = 11.2 Hz, 1 H), 4.57 (d, ^2J = 11.2 Hz, 1 H), 6.68 (d, ^3J = 8.3 Hz, 2 H), 6.73 (d, ^3J = 8.6 Hz, 2 H), 6.98 (d, ^3J = 8.3 Hz, 2 H), 7.81 (d, ^3J = 8.6 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 19.9 (CH_3), 20.4 (CH_3), 41.9 (CH_2), 54.7 (CH_3), 55.0 (CH_3), 68.4 (CH_2), 72.2 (C_q), 113.8 (2 × CH), 114.3 (2 × CH), 124.5 (2 × CH), 128.9 (C_q), 132.0 (2 × CH), 146.5 (C_q), 158.9 (C_q), 162.0 (C_q), 170.0 (C_q); MS (EI) *m*/*z* 356 (6) [M^+], 221 (31), 161 (46), 135 (100), 121 (48), 107 (84), 92 (5), 77 (12); HRMS (EI) calcd for $C_{20}H_{24}N_2O_4$ [M^+] 356.1736, found 356.1726.

3-(2,5-Dimethoxyphenyl)-2-(2,5-dimethoxyphenylazo)-2-methylpropan-1-ol (6q). Purification by column chromatography (P/EtOAc = 2:1 → 1:1) gave **6q** as a yellow oil: R_f = 0.60 (P/EtOAc = 1:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.46 (s, 3 H), 3.27 (s, 3 H), 3.33 (s, 3 H), 3.34 (d, ^2J = 13.5 Hz, 1 H), 3.37 (s, 6 H), 3.44 (d, ^2J = 13.5 Hz, 1 H), 3.93−3.98 (m, 2 H), 6.47 (d, ^3J = 9.0 Hz, 1 H), 6.55 (d, ^3J = 9.0 Hz, 1 H), 6.66 (dd, ^4J = 3.2 Hz, ^3J = 9.0 Hz, 1 H), 6.84 (dd, ^4J = 3.2 Hz, ^3J = 9.0 Hz, 1 H), 7.03 (d, ^3J = 3.2 Hz, 1 H), 7.25 (d, ^3J = 3.2 Hz, 1 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 20.6 (CH_3), 35.4 (CH_2), 55.2 (CH_3), 55.3 (CH_3), 55.5 (CH_3), 56.5 (CH_3), 67.3 (CH_2), 75.4 (C_q), 101.0 (CH), 111.7 (CH), 112.9 (CH), 114.6 (CH), 118.8 (CH), 118.9 (CH), 127.3 (C_q), 141.7 (C_q), 151.5 (C_q), 152.6 (C_q), 153.9 (C_q), 154.4 (C_q); MS (EI) *m*/*z* 374 (10) [M^+], 344 (47), 209 (22), 208 (11), 165 (32), 153 (29), 152 (18), 151 (100), 138 (19), 137 (14), 121 (29), 109 (12), 107 (16), 91 (10); HRMS (EI) calcd for $C_{20}H_{26}N_2O_5$ [M^+] 374.1842, found 374.1825.

(3-Phenyl-2-phenylazopropyl)carbamic Acid *tert*-Butyl Ester (6r). Purification by column chromatography (P/EtOAc = 10:1) gave **6r** as a yellow oil: R_f = 0.70 (P/EtOAc = 4:1); ^{1}H NMR (C_6D_6, 360 MHz) δ 1.38 (s, 9 H), 2.90 (dd, ^3J = 6.1 Hz, ^2J = 13.9 Hz, 1 H), 3.10 (dd, ^3J = 7.6 Hz, ^2J = 13.9 Hz, 1 H), 3.41−3.51 (m, 1 H), 3.57−3.64 (m, 1 H), 4.05−4.14 (m, 1 H), 4.40 (br s, 1 H), 6.92−7.08 (m, 8 H), 7.69 (d, ^3J = 6.8 Hz, 2 H); ^{13}C NMR (C_6D_6, 90 MHz) δ 28.4 (3 × CH_3), 37.8 (CH_2), 43.2 (CH_2), 78.7 (CH), 78.8 (C_q), 122.8 (2 × CH), 126.5 (CH), 128.6 (2 × CH), 129.1 (2 × CH), 129.8 (2 × CH), 130.7 (CH), 138.2 (C_q), 152.4 (C_q), 155.7 (C_q); MS (EI) *m*/*z* 339 (24) [M^+], 283 (92), 266 (20), 222 (28), 221 (33), 178 (48), 130 (30), 117 (32), 105 (47), 93 (100), 92 (37), 91 (57), 77 (52); HRMS (EI) calcd for $C_{20}H_{25}N_3O_2$ [M^+] 339.1947, found 339.1952.

2-(3-Hydroxy-2-oxopropyl)benzoic Acid Methyl Ester (17). To a solution of **6f** (220 mg, 0.55 mmol) in methanol (10 mL) was added potassium carbonate (96 mg, 0.70 mmol), and the resulting mixture was stirred for 2 h at room temperature. The mixture was diluted with water and extracted with dichloromethane (2×). The combined organic phases were dried over sodium sulfate and concentrated to give pure α-hydroxyhydrazone[10] (197 mg) in essentially quantitative yield. A solution of the hydrazone (150 mg, 0.42 mmol) in dioxane (5 mL) and water (0.5 mL) was then treated with oxalic acid dihydrate (700 mg, 5.55 mmol) and stirred at 70 °C for 4 h. The reaction mixture was diluted with water and extracted twice with ethyl acetate. The combined organic phases were washed with water and brine and dried over sodium sulfate. Purification by column chromatography (P/EtOAc = 3:1 → 2:1) gave **17** (67 mg, 0.32 mg, 77%) as a light yellow solid: R_f = 0.20 (P/EtOAc = 2:1); ^{1}H NMR ($CDCl_3$, 500 MHz,) δ 3.08 (br s, 1 H), 3.84 (s, 3 H), 4.06 (s, 2 H), 4.39 (s, 2 H), 7.24 (d, ^3J = 7.5 Hz, 1 H), 7.38 (dd, ^3J = 7.5 Hz, ^3J = 7.5 Hz, 1 H), 7.51 (dd, ^3J = 7.5 Hz, ^3J = 7.5 Hz, 1 H), 8.04 (d, ^3J = 7.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 44.8 (CH_2), 52.1 (CH_3), 68.0 (CH_2), 127.7 (CH), 128.8 (C_q), 131.2 (CH), 132.7 (2 × CH), 135.3 (C_q), 167.2 (C_q), 206.9 (C_q); MS (EI) *m*/*z* 208 (1) [M^+], 177 (100), 149 (98), 111 (39), 118 (24), 91 (44), 84 (58); HRMS (EI) calcd for $C_{10}H_9O_3$ [$M^+ - CH_3O$] 177.0552, found 177.0548.

Acetic Acid 2-[5-Methoxy-3-(4-methoxyphenyl)-1*H*-indol-2-yl]ethyl Ester (18). A solution of alcohol **6n** (210 mg, 0.67 mmol) in acetic acid was stirred at 90 °C for 6 h and was then concentrated under reduced pressure. The residue was dissolved in dichloromethane and washed with satd sodium carbonate, water, and brine. Drying over sodium sulfate, concentration under reduced pressure, and purification by column chromatography (P/EtOAc = 3:1) gave indole **18** (111 mg, 0.33 mmol, 49%) as an instable light brown oil: R_f = 0.60 (P/EtOAc = 2:1); ^{1}H NMR ($CDCl_3$, 360 MHz) δ 2.09 (s, 3 H), 3.14 (t, ^3J = 6.5 Hz, 2 H), 3.83 (s, 3 H), 3.89 (s, 3

H), 4.34 (t, ^3J = 6.5 Hz, 2 H), 6.87 (dd, ^4J = 2.5 Hz, ^3J = 8.6 Hz, 1 H), 7.04 (d, ^3J = 8.6 Hz, 2 H), 7.07 (d, ^3J = 2.5 Hz, 1 H), 7.24 (d, ^3J = 8.6 Hz, 1 H), 7.41 (d, ^3J = 8.6 Hz, 2 H), 8.31 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 21.0 (CH_3), 26.0 (CH_3), 52.2 (CH_3), 55.9 (CH_3), 63.8 (CH_2), 101.0 (CH), 111.3 (CH), 111.9 (CH), 114.1 (2 × CH), 115.2 (C_q), 127.2 (C_q), 128.2 (C_q), 130.4 (C_q), 130.6 (2×CH), 132.1 (C_q), 154.4 (C_q), 158.1 (C_q), 170.9 (C_q); MS (EI) *m/z* 339 (88) [M^+], 279 (78), 278 (68), 264 (51), 248 (100), 236 (28), 235 (49), 234 (26), 220 (22), 192 (22), 191 (16); HRMS (EI) calcd for $C_{20}H_{21}NO_4$ [M^+] 339.1471, found 339.1468.

4-Acetoxy-3-(4-methoxyphenylazo)-3-methylbutyric Acid (19). To a solution of azo compound **6p** (187 mg, 0.52 mmol) in CCl_4 (2 mL), CH_3CN (2 mL), and water (2.5 mL) were added sodium metaperiodate (1.60 g, 7.48 mmol) and $RuCl_3 \cdot H_2O$ (8 mg). After the mixture was stirred for 1.5 h at room temperature, additional CCl_4 (2 mL), CH_3CN (2 mL), and water (2.5 mL) as well as $RuCl_3 \cdot H_2O$ (4 mg) were added, and stirring was continued for another 2 h. The mixture was diluted with water and extracted twice with CH_2Cl_2. Drying over Na_2SO_4, concentration under reduced presssure, and purification by column chromatography ($CHCl_3$/MeOH = 7:1) gave azo compounds **6p** (42 mg, 0.12 mmol, 23%) and **19** (74 mg, 0.25 mmol, 48%) as yellow oils: R_f = 0.30 ($CHCl_3$/MeOH = 10:1); ^{1}H NMR ($CDCl_3$, 360 MHz) δ 1.44 (s, 3 H), 2.02 (s, 3 H), 2.82 (d, ^2J = 15.5 Hz, 1 H), 2.91 (d, ^2J = 15.5 Hz, 1 H), 3.86 (s, 3 H), 4.45 (d, ^2J = 11.2 Hz, 1 H), 4.58 (d, ^2J = 11.2 Hz, 1 H), 6.95 (d, ^3J = 9.0 Hz, 2 H), 7.68 (d, ^3J = 9.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 20.7 (CH_3), 20.8 (CH_3), 39.7 (CH_2), 55.6 (CH_3), 68.1 (CH_2), 69.9 (C_q), 114.1 (2 × CH), 124.2 (2 × CH), 145.4 (C_q), 162.1 (C_q), 170.7 (C_q); MS (ESI) *m/z* 295 [M^+ + H].

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Supporting Information Available: IR and ^{13}C NMR spectra for compounds **6a**−**r** and **17**−**19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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