Structural Features of Primary 6-Aminopentafulvenes and Some of Their Derivatives

Doris Kunz,[a] Roland Fröhlich,[a][‡] and Gerhard Erker*[a]

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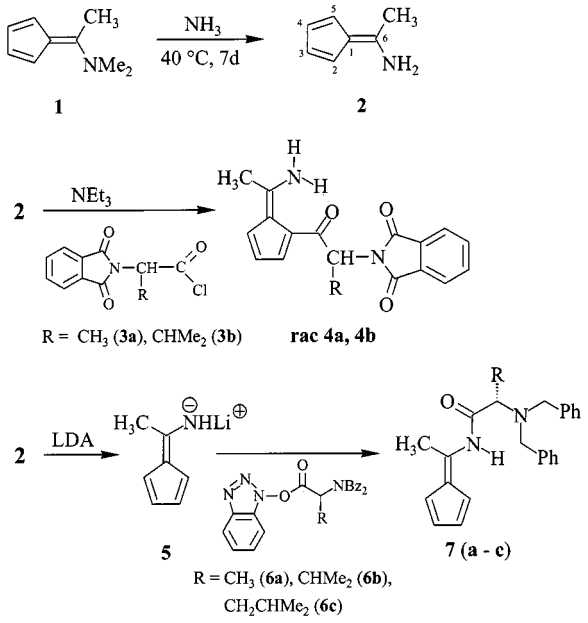
Starting from 6-amino-6-methylpentafulvene (**2**) "*ortho*"-*C*-acylation or *N*-acylation can be achieved selectively. Treatment of **2** with phthaloyl-protected amino acid chlorides derived from alanine (**3a**) or valine (**3b**) leads exclusively to the formation of the "*ortho*"-*C*-acylated derivatives **4**, isolated as racemates. Optically active *N*-acylated products **7** were prepared by coupling **5**, obtained by NH deprotonation of **2**, with the 1-hydroxybenzotriazole (HOBt) active-esters of alanine (**6a**), valine (**6b**), or leucine (**6c**) bearing benzyl-protected amino groups. Complexes **2**, **4a**, **4b**, and **7a** were characterized by X-ray diffraction. Electron-withdrawing groups attached at the "*ortho*" ring position lead to a shortening of the external C6–N bond, whereas electron-withdrawing groups bound to the nitrogen atom lead to an elongation of the C6–N bond, compared to the parent system **2**.

Introduction

Pentafulvenes are interesting starting materials in organic synthesis and especially in organometallic chemistry. The preparation of a great variety of cyclopentadienyl-type ligands that find increasing use in modern homogeneous catalysis relies on pathways based on pentafulvene systems.[1–16] Primary and secondary 6-aminopentafulvenes are of specific importance in this respect. They find use in the formation of bridged dianionic Cp/amido ligand systems, which are employed in the polymerization and copolymerization reactions of specific α-olefins.[17–21] Some of these Cp/amido anion or dianion equivalents, isolated and characterized as their alkali metal derivatives, exhibit interesting and at times rather unusual structural properties.[22,23] For a detailed understanding and discussion of some of their structural features it would be practical to compare them with neutral primary aminopentafulvenes. Surprisingly, the essential parent systems such as 6-amino-6-methylpentafulvene (**2**) seem not to have been characterized by X-ray diffraction so far, although these very useful organic compounds have been known for many years.[24] We, therefore, have characterized compound **2** (see Scheme 1) by X-ray crystal structure analysis, and we have prepared two series of derivatives of **2**, that contain electron-withdrawing substituents attached either at the carbocyclic ring system or the nitrogen center, and studied the systematic structural variations caused by these electronic consequences of the general 6-aminopentafulvene system. The preparations and the X-ray crystal structure analyses of these examples are described in this article along with a structural characterization of the parent 6-amino-6-methylpentafulvene **2**.



Scheme 1

Results and Discussion

The synthesis of 6-amino-6-methylpentafulvene (**2**) was carried out as described by Hafner et al.[24] For this purpose 6-(dimethylamino)-6-methylpentafulvene (**1**) was treated for a prolonged time (7 d) at elevated temperature (40 °C) with NH_3. In an addition/elimination reaction sequence the product **2** was formed by extrusion of dimethylamine.

The pentafulvene **2** was acylated to selectively yield two structural types of derivatives. Treatment of **2** with e.g. phthalimide-protected alanyl chloride (Pht-Ala-Cl, **3a**)[25–27] led to the exclusive formation of the "*ortho*"-*C*-acylated primary 6-aminofulvene derivative **4a**.[28–31] The ^{1}H NMR spectrum of the fulvene five-membered ring moiety exhibits an AMX-type pattern (δ = 7.62, 7.12, and 6.29) and a 1:1 pair of amino −NH− resonances. The latter

[a] Organisch-Chemisches Institut der Universität Münster, Corrensstrasse 40, 48149 Münster, Germany
Fax: (internat.) + 49-(0)251/833-6503
E-mail: erker@uni-muenster.de
[‡] X-ray crystal structure analyses.

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shows very different chemical shifts (δ = 7.44 and δ = 13.0) indicating the presence of a persistent $-NH\cdots O=C$ hydrogen bond under the conditions of the NMR measurement at ambient temperature. The presence of a favorable bicyclic internally hydrogen-bonded structure of **4a** is also evident from the IR spectrum (two NH bands of different intensities at $\tilde{\nu}$ = 3470 cm^{-1} and 3368 cm^{-1} and an acyl C=O band at $\tilde{\nu}$ = 1670 cm^{-1}) and the result of the X-ray crystal structure analysis (see below).

Treatment of **2** with Pht-Val-Cl (**3b**) gave the valine-derived aminopentafulvene derivative **4b**. Both the products **4a** and **4b** were obtained as racemates although their phthalimido-protected amino acid chloride precursors were optically active. The acylation procedure required trapping of the HCl co-product by adding triethylamine. It is likely that the products racemized rapidly under the applied basic reaction conditions during the time required for complete conversion of **2** to these α-acylated fulvene derivatives.

We next converted *N*,*N*-dibenzylalanine (Bn_2-Ala-OH)[32,33] into the active-ester **6a** by treatment with hydroxybenzotriazole/dicyclohexylcarbodiimide (HOBt/DCC).[34] The reagent **6a** turned out to be inactive towards coupling with the neutral 6-aminopentafulvene (**2**) under typical conditions; neither *C*- nor *N*-acylation could be achieved. Therefore, **2** was deprotonated by treatment with LDA. The resulting anion **5** turned out to be sufficiently nucleophilic to attack the activated Bn_2-Ala-OBt carbonyl group to selectively yield the respective amidofulvene derivative **7a** (Bn_2-Ala-NH-fulv). The obtained product is optically active. The analogous coupling reactions of **2** (via **5**) with the valine- or leucine-derived reagents **6b** and **6c** gave Bn_2-Val-NH-fulv (**7b**) and Bn_2-Leu-NH-fulv (**7c**), respectively, which are also optically active.

The compounds **2**, **4a**, **4b**, and **7a** were characterized by X-ray crystal structure analyses. Typical bond lengths of these compounds are listed in Table 1. Table 2 provides a compilation of structural data of selected other pentafulvene systems (see Scheme 2) for a comparison.

In the crystal 6-amino-6-methylpentafulvene (**2**, Figure 1) a close to symmetric alternating system of $C(sp^2)-C(sp^2)$ single and double bonds is exhibited. Inside the five-membered ring the lateral C2−C3 and C4−C5 bonds exhibit a pronounced C=C double bond character (ca. 1.36 Å) whereas their connecting C3−C4 bond is much longer at 1.42 Å. The C1−C2 and C1−C5 bonds inside the five-membered ring are also long (ca. 1.43 Å). The exocyclic C1−C6 double bond in **2** is slightly elongated at 1.388(2) Å, probably indicating a weak conjugative interaction with the attached $-NH_2$ substituent. Consequently, a C6−N bond length [1.345(2) Å] is observed for **2** that is in the typical range of a $C(sp^2)-N$ σ-bond.[35] The overall C_7N framework of **2** is planar as expected.

The *C*-acylated pentafulvenes **4a** (Figure 2) and **4b** (Figure 3) exhibit somewhat different structural features. The system **4a** contains a planar central framework with the $=C(NH_2)(CH_3)$ and the −COR moieties attached in "*ortho*", i.e. 1,2-positions at the five-membered ring. The $-NH_2$ substituent is oriented toward the acyl oxygen atom and is linked to it by means of a hydrogen bond. The typical fulvene bond alternation pattern is disturbed by this

Table 1. Selected structural data of primary 6-aminopentafulvene derivatives (bond lengths in Å, all structures this work)

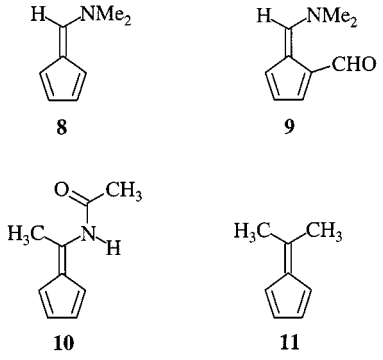
	2[a]	**4a**	**4b**[b]	**7a**[b]
C6−N	1.345(2)	1.299(4)	1.302(2)	1.385(14)
C6−C1	1.388(2)	1.410(5)	1.405(4)	1.308(14)
C1−C2	1.431(2)	1.454(5)	1.472(4)	1.431(15)
C2−C3	1.364(2)	1.402(4)	1.400(4)	1.354(15)
C3−C4	1.418(2)	1.391(5)	1.385(4)	1.441(16)
C4−C5	1.359(3)	1.369(5)	1.388(4)	1.315(15)
C1−C5	1.435(2)	1.410(4)	1.407(4)	1.459(16)

[a] Averaged values from the three independent molecules. − [b] Averaged from the two independent molecules.

Table 2. Selected structural parameters of *tert*-aminopentafulvenes and other substituted pentafulvenes for comparison (bond lengths in Å, for formulae of the compounds see Scheme 1)

	8	**9**[a]	**10**	**11**
C6−N	1.331(4)	1.309(4)	1.395(5)	−
C6−C1	1.387(4)	1.388(5)	1.359(5)	1.347(10)
C1−C2	1.427(4)	1.420(5)	1.447(5)	1.476(8)
C2−C3	1.362(5)	1.376(5)	1.348(5)	1.340(6)
C3−C4	1.414(5)	1.392(5)	1.428(6)	1.462(9)
C4−C5	1.353(5)	1.387(5)	1.339(5)	1.340(6)
C1−C5	1.438(4)	1.449(4)	1.462(5)	1.476(8)
Ref.	[36]	[36]	[17]	[37]

[a] Averaged values from two independent molecules in the crystal.



Scheme 2

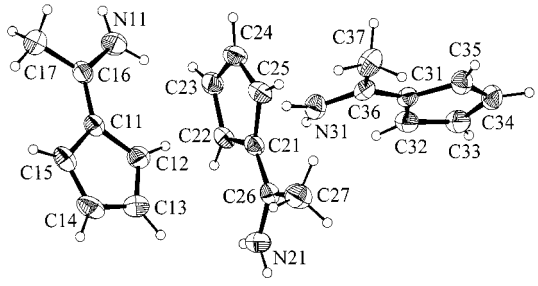


Figure 1. A projection of the three independent molecules of **2** in the crystal

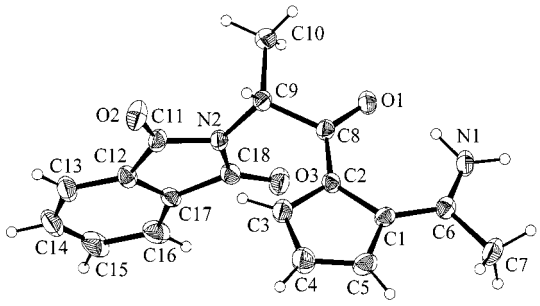


Figure 2. Molecular geometry of **4a**

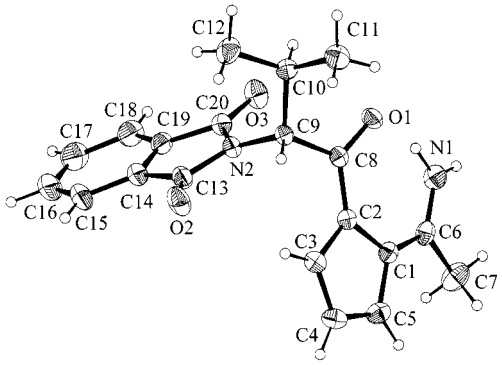
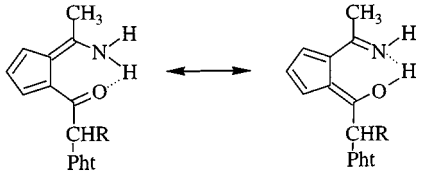


Figure 3. A projection of the molecular geometry of **4b**



4 **4'**

Scheme 3

arrangement. Compound **4a** features a longer C1−C6 bond [1.410(5) Å] and a markedly shorter C6−N bond length [1.299(4) Å] as compared to the parent compound **2**. Consequently, the C2−C3 bond in **4a** [1.402(4) Å] is markedly longer than in **2** (see Table 1), and the C3−C4 bond [1.391(5) Å] in **4a** is shorter than the respective bond in **2** [1.418(2) Å]. The overall bonding pattern in the compounds **4a** and **4b** indicates a contribution of the resonance hybrids **4′** (see Scheme 3) for the description of these substituted pentafulvenes, although the C8−O double bond is only marginally elongated [1.237(4) Å for **4a**]. The C1−C2 bond is the longest inside the five-membered ring [**4a**: 1.454(5) Å] as is expected for the **4** ↔ **4′** resonance hybrid. In both structures there is a weak intermolecular hydrogen bond between the "*exo*"-positioned −NH and one phthaloyl carbonyl oxygen atom.

The *N*-acylated system **7a** shows the typical alternation of the cross-conjugated π-system (see Figure 4 and Table 1). In **7a** the carboxamide formation has markedly diminished the ability of the electron lone pair at the nitrogen atom to electronically interact with the pentafulvene π-system. Consequently, the C6−N bond in **7a** at 1.385(14) Å is even longer than it was found in the parent aminopentafulvene

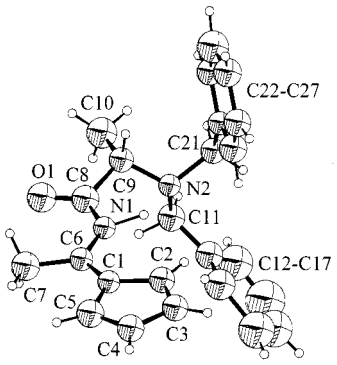


Figure 4. Molecular structure of **7a** (isotropic thermal displacement parameter with 30% probability)

2, and the adjacent exocyclic C1−C6 double bond is shorter at 1.308(14) Å.

A comparison of the structural features of the unsubstituted 6-aminopentafulvene **2** with e.g. 6-dimethylaminopentafulvene **8**[36,37] (see Table 1 and Table 2) reveals that the primary aminopentafulvene and the *tert*-aminopentafulvene have very similar structural parameters. The pentafulvene exhibits a typical bond alternating cross-conjugated π-system. The structural consequences of the $-NH_2$ lone-pair/C=C π-interaction are marginal. Electron-withdrawing substituents at the amino nitrogen atom (such as found in **7** or **10**, see Scheme 2) further reduce the C6−N bond order and lead to an increased C6−N separation from the typical 1.345(2) Å in the unsubstituted parent 6-aminopentafulvene **2** to almost 1.40(1) Å in the *N*-acyl derivatives (see Table 1 and Table 2). The attachment of an electron-withdrawing carbonyl functionality in the "*ortho*" position at the fulvene five-membered ring has an opposite effect: the nitrogen center of the 6-amino group helps to fill in the electron demand of the central fulvene system by mesomeric interaction, which results in a marked shortening of the peripheral C6−N bond lengths in **4a** and **4b** to ca. 1.30(1) Å. A comparison of the structures of the parent compound **2** with e.g. its relatives **8** and **11**[37] (see Scheme 2, Table 1 and Table 2) shows that amino substituents at C-6 of the unsubstituted pentafulvenes do not seem to lead to marked alterations of the typical fulvene structural features. However, in conjunction with the presence of additional electron-withdrawing groups, either attached at the nitrogen atom or at suitable carbon positions, the structural fulvene characteristics can be altered substantially.

Experimental Section

Solvents used for the preparation of the pentafulvene derivatives were dried and distilled under argon prior to use. The reagents **1**, **3a**, and **3b** were prepared according to the literature.[24,38] *N*,*N*-Dibenzylalanine, -valine, and -leucine used for the generation of the reagents **6a**, **6b**, and **6c** were synthesized as described in the literature.[32,33] − For instrumentation used for the characterization of the compounds, including a list of spectrometers used, see e.g. ref.[39] Most NMR assignments were secured by 2D experiments

(e.g. GCOSY, GHSQC, GHMBC).[40] A (nonsystematic) atom numbering scheme is used as in Figure 1.

6-Amino-6-methylpentafulvene (2): Preparation analogous to a procedure described previously by Hafner et al.[24] A steel autoclave was charged with 6-dimethylamino-6-methylpentafulvene (**1**), and then precooled (−78 °C) liquid NH_3 (ca. 200 mL) was carefully added at −78 °C. The reaction mixture was kept for 7 d at 40 °C (resulting pressure: ca. 15 bar). The autoclave was then cooled again to −78 °C, opened, and the ammonia slowly evaporated into dilute aqueous sulfuric acid. The remaining solid was dried in vacuo to given 25.3 g (98%) of **2** that was not further purified when used in subsequent reactions. − ^{1}H NMR (200.1 MHz, $CDCl_3$, 300 K): δ = 6.56−6.29 (m, 4 H, 2-H to 5-H), 5.11 (br. s, 2 H, NH_2), 2.31 (s, 3 H, 7-H). − ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ = 155.0 (C6), 124.4, 121.9, 119.6, 112.3 (C2 to C5), 117.8 (C1), 19.5 (CH_3).

X-ray Crystal Structure Analysis of 2: Empirical formula C_7H_9N, M = 107.15, yellow crystal 0.80 × 0.35 × 0.10 mm, a = 10.151(1), b = 10.749(1), c = 10.970(1) Å, α = 67.36(1), β = 68.25(1), γ = 64.92(1)°, V = 969.3(2) Å^3, $\rho_{calcd.}$ = 1.101 g·cm^{-3}, μ = 0.65 cm^{-1}, empirical absorption correction via SORTAV (0.950 ≤ T ≤ 0.994), Z = 6, triclinic, space group $P\bar{1}$ (No. 2), λ = 0.71073 Å, T = 198 K, ω and φ scans, 10337 reflections collected (±h, ±k, ±l), (sinθ)/λ = 0.67 Å^{-1}, 4548 independent (R_{int} = 0.048) and 2913 observed reflections [$I \geq 2\,\sigma(I)$], 217 refined parameters, R = 0.053, wR^2 = 0.148, max. residual electron density 0.17 (−0.21) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

***rac*-6-Amino-6-methyl-2-(*N*-phthaloylalaninyl)pentafulvene (4a):** A Schlenk flask was charged with a solution of **3a** (1.84 g, 7.75 mmol) in toluene (50 mL) and cooled to 0 °C. A precooled (0 °C) solution of the aminofulvene **2** (830 mg, 7.75 mmol) and triethylamine (2.15 mL, 15.5 mmol) in THF (20 mL) was slowly added, whereupon a white precipitate appeared. The suspension was allowed to warm to room temperature and stirred overnight. The precipitate was removed by filtration and the solvent evaporated from the clear filtrate in vacuo. Remaining triethylammonium chloride was removed by taking up the remaining solid in ethyl acetate (70 mL) and extracting it with water (3 × 20 mL). The organic phase was dried with magnesium sulfate and the solvent removed in vacuo. The remaining precipitate was washed with pentane (20 mL) to give 1.26 g (53%) of **4a**, m.p. 193 °C (DSC). − $[\alpha]_D^{25}$ = 0. − ^{1}H NMR (599.8 MHz, $CDCl_3$, 303 K): δ = 12.7 (br. s, 1 H, N*H* bonding), 7.80 (m, 2 H, phth. 3,6-H), 7.69 (m, 2 H, phth. 4,5-H), 7.38 (dd, ^3J = 3.7, ^4J = 1.9 Hz, 1 H, fulv. 3-H), 7.06 (dd, ^3J = 4.1, ^4J = 1.9 Hz, 1 H, fulv. 5-H), 6.9 (br. s, 1 H, NH), 6.27 (pseudo-t, 1 H, fulv. 4-H), 5.86 (q, ^3J = 7.3 Hz, 1 H, ala-C*H*), 2.49 (s, 3 H, fulv. 6-CH_3), 1.83 (d, ^3J = 7.3 Hz, 3 H, ala-CH_3). − ^{13}C NMR (150.8 MHz, $CDCl_3$, 303 K): δ = 189.1 (ala C=O), 168.3 (phth. C=O), 165.4 (fulv. C6), 133.9 (phth. C4,5), 133.4 (fulv. C3), 132.0 (fulv. C5), 131.5 (phth. C1,6), 123.2 (phth. C3,6), 122.1 (fulv. C2), 117.9 (fulv. C4), 117.2 (fulv. C1), 51.6 (ala *C*H), 21.7 (fulv. CH_3), 16.8 (ala CH_3). − IR (KBr): ṽ = 3382 (s), 3090 (w), 1776 (s), 1764 (m), 1710 (vs), 1658 (s) 1593 (vs) cm^{-1}. − MS (70 eV): *m*/*z* (%) = 308 (18) [M$^+$], 134 (100). − HRMS (70 eV): *m*/*z* calcd. for $C_{18}H_{16}N_2O_3$ 308.1161, found 308.1155.

X-ray Crystal Structure Analysis of 4a: Single crystals were obtained by diffusion of *n*-hexane vapor into a solution of the **4a** (30 mg) racemate in chloroform (0.5 mL) at ambient temperature. Empirical formula $C_{18}H_{16}N_2O_3$, M = 308.33, yellow crystal 0.20 × 0.10 × 0.10 mm, a = 7.942(1), b = 10.430(2), c = 10.714(2) Å, α = 117.28(2), β = 103.12(2), γ = 90.47(2)°, V = 761.7(2) Å^3, $\rho_{calcd.}$ = 1.344 g·cm^{-3}, μ = 0.93 cm^{-1}, empirical absorption correction via ψ scan data (0.982 ≤ T ≤ 0.991), Z = 2, triclinic, space group $P\bar{1}$ (No. 2), λ = 0.71073 Å, T = 223 K, ω/2θ scans, 2846 reflections collected (±h, ±k, +l), (sinθ)/λ = 0.59 Å^{-1}, 2689 independent (R_{int} = 0.040) and 1109 observed reflections [$I \geq 2\,\sigma(I)$], 208 refined parameters, R = 0.051, wR^2 = 0.100, max. residual electron density 0.21 (−0.18) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

***rac*-6-Amino-6-methyl-2-(*N*-phthaloylvalinyl)pentafulvene (4b):** Analogously as described above, **3b** (1.72 g, 6.49 mmol) in toluene (50 mL) was treated with **2** (695 mg, 6.49 mmol) and triethylamine (1.80 mL, 13.0 mmol) in THF (20 mL) at 0 °C. After stirring overnight at room temperature, a precipitate was removed by filtration, the solution washed with water (4 × 10 mL) and dried with magnesium sulfate. Solvent was removed in vacuo and the resulting solid washed with pentane (20 mL) to give 1.60 g (73%) of **4b**, m.p. 173 °C (DSC). − $[\alpha]_D^{25}$ = 0. − ^{1}H NMR (599.8 MHz, $CDCl_3$, 300 K): δ = 13.0 (br. s, 1 H, N*H* bonding), 7.79 (m, 2 H, phth. 3,6-H), 7.65 (m, 2 H, phth. 4,5-H), 7.62 (dd, ^3J = 3.6, ^4J = 1.8 Hz, 1 H, fulv. 3-H), 7.44 (br. s, 1 H, NH), 7.12 (dd, ^3J = 4.2 Hz, ^4J = 1.8 Hz, fulv. 5-H), 6.29 (pseudo-t, 1 H, fulv. 4-H), 5.39 (d, ^3J = 10.8 Hz, 1 H, val CO-C*H*), 3.18 (d, sept, ^3J = 10.8 Hz and 6.6 Hz, 1 H, val Me_2C*H*), 2.59 (s, 3 H, fulv. CH_3), 1.02 and 0.94 (each d, ^3J = 6.6 Hz, each 3 H, val CH_3). − ^{13}C NMR (150.8 MHz, $CDCl_3$, 300 K): δ = 187.7 (val-C=O), 168.2 (phth. C=O), 165.7 (fulv. C6), 134.4 (fulv. C3), 133.9 (phth. C4,5), 132.2 (fulv. C5), 131.6 (phth. C1,2), 124.6 (fulv. C2), 123.2 (phth. C3,6), 117.7 (fulv. C4), 117.3 (fulv. C1), 60.9 (val CO-*C*H), 26.6 (val *C*HMe_2), 21.7 (fulv. CH_3), 20.6 and 19.3 (val CH_3). − IR (KBr): ṽ = 3368 (vs), 3089 (w), 1769 (s), 1712 (vs), 1670 (s), 1595 (vs) cm^{-1}. − MS (70 eV): *m*/*z* (%) = 336 (16) [M$^+$]. 134 (100). − HRMS (70 eV): calcd. for $C_{20}H_{20}N_3O_3$: 336.1474, found 336.1465. − $C_{20}H_{20}N_2O_3$ (336.4): calcd. C 71.41, H 5.99, N 8.33; found C 71.26, H 6.17, N 8.27.

X-ray Crystal Structure Analysis of 4b: Single crystals were obtained from diethyl ether at −18 °C. Empirical formula $C_{20}H_{20}N_2O_3$, M = 336.38, light yellow crystal 0.15 × 0.10 × 0.05 mm, a = 9.458(1), b = 14.712(1), c = 15.534(1) Å, α = 116.81(1), β = 105.05(1), γ = 94.49(1)°, V = 1814.5(4) Å^3, $\rho_{calcd.}$ = 1.231 g·cm^{-3}, μ = 6.77 cm^{-1}, empirical absorption correction via ψ scan data (0.905 ≤ T ≤ 0.967), Z = 4, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, T = 223 K, ω/2θ scans, 7710 reflections collected (±h, −k, ±l), (sinθ)/λ = 0.62 Å^{-1}, 7408 independent (R_{int} = 0.061) and 3849 observed reflections [$I \geq 2\,\sigma(I)$], 452 refined parameters, R = 0.053, wR^2 = 0.128, max. residual electron density 0.24 (−0.21) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Preparation of the *N*,*N*-Dibenzyl-Protected *N*-Amino Acid Substituted Pentafulvenes 7. − General Procedure

a) Preparation of the Active-Esters: The respective *N*,*N*-dibenzyl-protected amino acid (10 mmol) was suspended at 0 °C in dichloromethane (100 mL) together with hydroxybenzotriazole (HOBt) (1.35 g, 10 mmol). Then dicyclohexylcarbodiimide (DCC) (2.06 g, 10 mmol) was added and the mixture stirred for 1 h at 0 °C to precipitate the dicyclohexylurea co-product. This was removed by filtration and the solvent was removed from the filtrate to yield the respective active-ester as a colorless viscous oil.

b) Lithiation of 6-Amino-6-methylpentafulvene (2). − Formation of 5: LDA (1.07 g, 10 mmol) and **2** (1.07 g, 10 mmol) were co-dissolved in diethyl ether (50 mL) at −30 °C. The cooling bath was removed and the mixture allowed to warm to room temperature with stirring. After 10 min at ambient temperature, the solvent and

the formed diisopropylamine were removed in vacuo to give **5** as a solid.

c) Reaction of 5 with the Active-Esters 6a−c: The respective active-ester (see above) was dissolved in diethyl ether (100 mL) and treated at 0 °C with **5** (see above), dissolved in diethyl ether (50 mL). The reaction mixture was allowed to slowly warm to room temperature and stirred for 12 h. The precipitated lithium chloride was removed by filtration and the solvent removed from the filtrate in vacuo. The resulting product was purified by silica gel flash chromatography.

Preparation of Bn_2-Ala-NH-fulv (7a): L-*N*,*N*-Dibenzylalanine (4.00 g, 14.9 mmol) was treated with HOBt (2.01 g, 14.8 mmol) and DCC (3.06 g, 14.9 mmol) as described above to give **6a** which was then treated with **5**, generated by treatment of **2** (1.59 g, 14.8 mmol) with LDA (1.59 g, 14.8 mmol) to give **7a**, which was isolated after flash chromatography (silica gel, diethyl ether/pentane 1:12 + 1 vol-% of dimethylethylamine) as a yellow viscous oil. Yield of **7a**: 3.63 g (68%). From the oil single crystals were obtained after 1 week that were used for the X-ray crystal structure analysis (see below), m.p. 59 °C (DSC). − $[\alpha]_D^{20}$ = −174 (*c* = 0.2, dichloromethane). − ^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ = 9.94 (br. s, 1 H, NH), 7.31−7.17 (m, 10 H, Ph), 6.53 (m, 1 H, fulv. 5-H), 6.46 (m, 1 H, fulv. 3-H), 6.44 (m, 1 H, fulv. 2-H), 6.37 (m, 1 H, fulv. 4-H), 3.73 and 3.35 (AB, ^2J = 12.8 Hz, 4 H, benzyl), 3.41 (q, ^3J = 6.4 Hz, 1 H, ala C*H*), 2.61 (s, 3 H, fulv. CH_3), 1.27 (d, ^3J = 6.4 Hz, 3 H, ala CH_3). − ^{13}C NMR (100 MHz, $CDCl_3$, 300 K): δ = 172.5 (C=O), 145.3 (fulv. C6), 137.9 (*ipso*-C of Ph), 129.4 (fulv. C3), 129.1 (*o*- or *m*-Ph), 128.8 (*o*- or *m*-Ph), 128.2 (fulv. C2), 127.7 (*p*-Ph and fulv. C1), 121.6 (fulv. C5), 114.7 (fulv. C2), 58.6 (ala *C*H), 54.7 (*C*H_2Ph), 18.2 (fulv. CH_3), 6.5 (ala CH_3). − IR (KBr): $\tilde{\nu}$ = 3314 (w), 1722 (vs), 1617 (s) cm^{-1}. − UV/Vis (dichloromethane): λ_{max} (ε) = 232 nm (5000), 324 nm (24500). − $C_{24}H_{26}N_2O$ (358.5): calcd. C 80.41, H 7.31, N 7.81; found C 79.52, H 7.46, N 7.82.

X-ray Crystal Structure Analysis of 7a: Empirical formula $C_{24}H_{26}N_2O$, *M* = 358.47, yellow crystal 0.20 × 0.15 × 0.10 mm, *a* = 23.606(4), *b* = 14.423(1), *c* = 16.332(3) Å, β = 131.53(2)°, *V* = 4162.7(11) Å^3, $\rho_{calcd.}$ = 1.144 g·cm^{-3}, μ = 5.43 cm^{-1}, empirical absorption correction via ψ scan data (0.899 ≤ *T* ≤ 0.948), *Z* = 8, monoclinic, space group *C*2 (No. 5), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 3082 reflections collected (±*h*, −*k*, +*l*), (sinθ)/λ = 0.55 Å^{-1}, 2962 independent (R_{int} = 0.051) and 1086 observed reflections [*I* ≥ 2 σ(*I*)], 217 refined parameters, *R* = 0.088, wR^2 = 0.206, max. residual electron density 0.32 (−0.21) e·Å^{-3}, due to the weakly diffracting crystal and the resulting small amount of observed reflections the structure was refined with isotropic thermal parameters, hydrogen atoms calculated and refined as riding atoms.

Data sets were collected with Nonius CAD4 and KappaCCD diffractometers; in case of Mo radiation a rotating anode generator Nonius FR591 was used. Programs used: for data collection: EXPRESS (Nonius B.V., 1994) and COLLECT (Nonius B.V., 1998), for data reduction: MolEN (K. Fair, Enraf−Nonius B.V., **1990**) and Denzo-SMN (Z. Otwinowski, W. Minor, *Methods Enzymol.*, **1997**, *276*, 307−326), for absorption correction for CCD data: SORTAV (R. H. Blessing, *Acta Crystallogr.* **1995**, *A51*, 33−37; R. H. Blessing, *J. Appl. Cryst.* **1997**, *30*, 421−426), for structure solution: SHELXS-97 (G. M. Sheldrick, *Acta Crystallogr.* **1990**, *A46*, 467−473), for structure refinement: SHELXL-97 (G. M. Sheldrick, Universität Göttingen, **1997**), for graphics DIAMOND (K. Brandenburg, Universität Bonn, **1997**).

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publications CCDC-155728−155731. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033, E-mail: deposit@ccdc.cam.ac.uk].

Preparation of Bn_2-Val-NH-fulv (7b): Analogously as described above, L-Bn_2-Val-OH (7.46 g, 25.0 mmol) was converted into **6b** by treatment with HOBt (3.40 g, 25.0 mmol) and DCC (5.16 g, 25.0 mmol) in diethyl ether (100 mL). The reagent **5** was generated by treatment of **2** (2.46 g, 23.0 mmol) with LDA (2.47 g, 23.0 mmol). The solution of **5** in diethyl ether (30 mL) was then treated with **6b**. Workup as described above followed by flash chromatography on silica gel with diethyl ether/pentane (1:20, + 1 vol-% of dimethylethylamine) gave **7b** (1.67 g, 19%) as a yellow oil. − $[\alpha]_D^{20}$ = +100 (*c* = 0.2, dichloromethane). − ^{1}H NMR (400.1 MHz, [D_6]benzene, 300 K): δ = 7.93 (br. s, 1 H, NH), 7.32 (m, 4 H, *o*-Ph), 7.18 (m, 4 H, *m*-Ph), 7.07 (m, 2 H, *p*-Ph), 6.59 (m, 1 H, fulv. 5-H), 6.57 (m, 1 H, fulv. 3-H), 6.51 (m, 1 H, fulv. 4-H), 6.39 (m, 1 H, fulv. 2-H), 3.92 and 3.45 (AB, ^2J = 14.4 Hz, 4 H, CH_2Ph), 2.70 (d, ^3J = 9.2 Hz, 1 H, val C*H*CO), 2.66 (s, 3 H, fulv. CH_3), 2.17 (m, 1 H, val C*H*Me_2), 1.01 and 0.66 (each d, ^3J = 6.8 Hz, each 3 H, val CH_3). − ^{13}C NMR (100.6 MHz, [D_6]benzene, 300 K): δ = 170.1 (C=O), 144.5 (fulv. C6), 139.5 (*ipso*-C of Ph), 130.2 (fulv. C3), 129.10 (fulv. C1), 129.02 (fulv. C4), 128.97 (*o*-Ph), 128.9 (*m*-Ph), 127.6 (*p*-Ph), 122.3 (fulv. C5), 114.8 (fulv. C2), 70.6 (val C*H*CO), 54.9 (*C*H_2Ph), 27.4 (val *C*HMe_2), 20.1 and 19.7 (val CH_3), 18.6 (fulv. CH_3). − IR (KBr): $\tilde{\nu}$ = 3370 (w), 1678 (vs), 1631 (vs) cm^{-1}. − $C_{26}H_{30}N_2O$ (386.5): calcd. C 80.79, H 7.82, N 7.25, found C 80.73, H 8.01, N 7.02%.

Preparation of Bn_2-Leu-NH-fulv (7c): L-*N*,*N*-Dibenzylleucine (15.0 g, 48.2 mmol) was treated with HOBt (6.51 g, 48.2 mmol) and DCC (9.94 g, 48.2 mmol) analogously as described above and the product then treated with **5**, generated by treatment of **2** (5.16 g, 48.2 mmol) with LDA (5.16 g, 48.2 mmol). The product was flash-chromatographed on silica gel with diethyl ether/pentane (1:30, + 1 vol-% of dimethylethylamine) to yield **7c** as a yellow oil (5.91 g, 31%). − $[\alpha]_D^{20}$ = −101 (*c* = 0.2, dichloromethane). − ^{1}H NMR (400.1 MHz, $CDCl_3$, 300 K): δ = 9.68 (br. s, 1 H, NH), 7.37−7.26 (m, 10 H, Ph), 6.62 (m, 1 H, fulv. 5-H), 6.55 (m, 1 H, fulv. 3-H), 6.51 (m, 1 H, fulv. 2-H), 6.46 (m, 1 H, fulv. 4-H), 3.79 and 3.47 (AB, ^2J = 13.2 Hz, 2 H, CH_2-Ph), 3.31 (dd, ^3J = 9.6 and 2.4 Hz, 1 H, leu C*H*CO), 2.72 (s, 3 H, fulv. CH_3), 1.98 (ddd, ^2J = 13.2 Hz, ^3J = 9.6 and 4.0 Hz, 1 H, leu CH_2), 1.83 (m, 1 H, leu C*H*Me_2), 1.48 (ddd, ^2J = 13.2 Hz, ^3J = 10.0 and 2.4 Hz, 1 H, leu CH_2), 1.04 (d, ^3J = 6.4 Hz, 3 H, leu CH_3), 0.90 (d, ^3J = 6.8 Hz, 3 H, leu CH_3). − ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K): δ = 172.5 (C=O), 145.6 (fulv. C6), 138.3 (*ipso*-C of Ph), 129.3 (fulv. C3), 129.2 (*o*- or *m*-Ph), 128.7 (*o*- or *m*-Ph), 128.1 (fulv. C4), 127.7 (*p*-Ph and fulv. C1), 121.7 (fulv. C5), 114.7 (fulv. C2), 61.4 (leu CO*C*H), 54.7 (*C*H_2Ph), 32.3 (leu CH_2), 26.4 (leu *C*HMe_2), 23.8 and 21.9 (leu CH_3), 18.3 (fulv. CH_3). − IR (KBr): $\tilde{\nu}$ = 3334 (vw), 1743 (m), 1641 (m) cm^{-1}. − $C_{27}H_{32}N_2O$ (400.6): calcd. C 80.96, H 8.05, N 6.99, found C 80.08, H 7.87, N 6.61%.

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