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Utilization of 1-phenylimidazo[1,5-*a*]quinoline as partner in 1,4-dipolar cycloaddition reactions

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Abstract: A Selected set of 2-(quinolin-2-yl)-1,3-oxazepino[7,6-*b*]indoles **4a–d** and dihydroacenaphtho[1,2-*f*][1,3]oxazepine **5** have been prepared via 1,4-dipolar cycloaddition reaction involving 1-phenylimidazo[1,5-*a*]quinoline, dimethyl acetylenedicarboxylate, and *N*-(substituted)isatins or acenaphthoquinone. Structures of the new heterocycles **4a–d** and **5** are supported by NMR and HRMS spectral data, and confirmed by single-crystal X-ray crystallography for **4c** and **5**.

Keywords: 1-phenylimidazo[1,5-*a*]quinoline; 1,4-dipolar cycloaddition; acenaphthoquinone; dimethyl acetylenedicarboxylate; *N*-methylisatin; *N*-phenylisatin.

1 Introduction

Multicomponent reactions (MCRs), in which three or more reactants are connected sequentially in a one-pot reaction, have attracted considerable attention owing to high synthetic efficiency and the facile construction of complex organic molecules [1–13]. 1,4-Dipolar cycloaddition, a subclass of MCRs, emerged as a convenient route towards the synthesis of a variety of six-membered *N*-heterocycles, exemplified by **I** (Fig. 1). The latter spiro-derivative is produced utilizing dimethyl acetylenedicarboxylate (DMAD), pyridine and *N*-methylisatin; herein, the 1,4-dipolar zwitter ion **II** [14, 15] (Fig. 1) was suggested as transient intermediate arising from nucleophilic addition of the pyridine nitrogen onto DMAD. Interaction of various

N-heteroarenes and dipolarophiles, together with DMAD, were successfully applied for attainment of the respective spiro-1,3-oxazino heterocycles, and the subject was reviewed [15].

Quite recently, we have applied this reaction in the synthesis of 1,3-oxazepino[7,6-*b*]indoles **III** (Fig. 1) utilizing imidazo[1,5-*a*]pyridines, DMAD and isatins [16]. We sought it would be worthwhile to utilize other *N*-bridgehead-imidazo heterocycles (in placement of imidazo[1,5-*a*]pyridines) so as to widen the scope and applicability of this new reaction towards the synthesis of novel tricyclic and tetracyclic products.

Accordingly, the present work aims at the synthesis of a selected set of model 2-(quinolin-2-yl)-1,3-oxazepino[7,6-*b*]indoles **4a–d** and dihydroacenaphtho[1,2-*f*][1,3]oxazepine **5**, utilizing 1-phenylimidazo[1,5-*a*]quinoline, DMAD, and substituted isatins or acenaphthoquinone as illustrated in Schemes 1–3 (*vide infra*).

2 Results and discussion

2.1 Synthesis

The formation of compounds **4a–d** most logically proceeds via the intermediacy of the spiro cyclo-adduct **[B]**, produced via cycloaddition of the 1,4-dipolar zwitter ion **[A]** and the dipolarophilic keto group of the respective isatin (Scheme 2). Adducts **[B]** then suffer intramolecular skeletal rearrangement involving a cascade of bond-breaking and bond-making processes (**[B]**→**[C]**→**[D]**), leading to the respective end products as depicted in the postulated mechanism (Scheme 2). As a consequence, the dihydroquinoline ring in spiro adducts **[B]** restores aromaticity whilst the spiro oxindole entity acquires the status of indolic system conjugated with the maleate moiety; such events represent the driving force for the conversion of the spiro adducts **[B]** into oxazepino[7,6-*b*]indoles **4a–d**. This mechanism is essentially similar to that previously reported by us for related systems [16].

In its reaction with imidazo[1,5-*a*]quinoline and DMAD, acenaphthoquinone (an arene-*vic*-dione)

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Fig. 1: Structures I–III.

Scheme 1: Formation of 2-(quinolin-2-yl)-1,3-oxazepino[7,6-b]indoles **4a–d**.

followed an 1,4-dipolar cycloaddition path similar to that of isatins **3** and yielded the respective dihydroacenaphtho[1,2-f][1,3]oxazepine **5** as the end product (Scheme 3).

The new compounds **4a–d** and **5** were characterized by MS and NMR spectral data. These data, detailed in the experimental section, are consistent with the suggested structures. Thus, the mass spectra display the

correct molecular ion peaks for which the measured high resolution (HRMS) data are in good agreement with the calculated values. DEPT and 2D (COSY, HMQC, HMBC) experiments showed correlations that helped in the ^1H and ^{13}C signal assignments to the different carbons and their attached and/or neighboring hydrogens. For compound **4c**, the carbons of the benzo-fused ring are readily identified by their doublet signals (with varying J values)

Scheme 2: Postulated mechanism for the formation of oxazepino[7,6-*b*]indoles **4a–d**.

Scheme 3: Formation of dihydroacenaphtho[1,2-*f*][1,3]oxazepine **5**.

originating from coupling with the nearby fluorine atom at C-5. Eventually, the structures of **4c** (a representative of the present set) and **5** are confirmed by single-crystal X-ray crystallography (Figs. 2 and 3; *vide infra*).

The quinoline ring at C-2 might in part have interesting biological properties to the oxazepino[7,6-*b*]indoles **4a–d** and dihydroacenaphtho[1,2-*f*][1,3]oxazepine **5**. This follows from the fact that the quinoline nucleus occurs

naturally in quinoline alkaloids with diverse biological activities [17].

2.2 Molecular structures of **4c** and **5**

Crystal structure determinations were performed to confirm the structures of **4c** and **5**. Crystal data and a

Fig. 2: Molecular structure of **4c** in the crystal (displacement ellipsoids at the 30% probability level, H atoms as spheres with arbitrary radii).

summary of data collection and refinement parameters for **4c** and **5** are given in Table 1, while selected sets of bond lengths and bond angles for **4c** and **5** are provided in Tables 2 and 3, respectively. The molecular structures of **4c** and **5** in the crystal are shown in Figs. 2 and 3.

The crystal structure data of compounds **4c** and **5** reveal slight deviations from mean planarity of the seven-membered rings. The most deviating atoms from planarity are the sp^3 -hybridized N3 and C2 atoms with values of -0.539 and 0.267 Å for compound **4c**; a comparable deviation is also observed in compound **5** for the sp^3 -hybridized atoms N9 and C8 with values of -0.351 and 0.600 Å. A remarkable mutual interaction is observed in compound **4c** between O4 (of the carbonyl group at C4) and C31 of the adjacent carbonyl ester as is evident from the close proximity of the two atoms, with a separation of only 2.58 Å, a value which is 0.640 Å less than the sum of their van der Waals radii. A comparable trend is also observed in compound **5** for the atoms O29 (of carbonyl group at C11)

and C32 of the adjacent carbonyl ester, with a separation of only 2.597 Å, a value which is 0.623 Å less than the sum of their van der Waals radii. This interaction seems to force both carbonyl esters to acquire almost perpendicular arrangement to one another with a dihedral angle of 87.54° between C27–O4–O3–C30 and the C31–O5–O6–C34 planes for compound **4c**, while for compound **5** the dihedral angle of 73.45° is observed between the planes C28–O29–O30–C31 and C32–O33–O34–C35.

3 Experimental section

Dimethyl acetylenedicarboxylate (DMAD), quinoline-2-carbaldehyde, 5-methoxyisatin, 5-fluoroisatin, *N*-phenylisatin, acenaphthoquinone and dry dichloromethane were purchased from Acros. (Geel, Belgium). Melting points (uncorrected) were determined on a Gallenkamp electrothermal melting temperature apparatus (London,

Fig. 3: Molecular structure of **5** in the crystal (displacement ellipsoids at the 30% probability level, H atoms as spheres with arbitrary radii, co-crystallized molecules EtOAc not drawn).

UK) in open capillary tubes. ^1H , ^{13}C NMR spectra, and 2D (COSY, HMQC, HMBC) experiments were recorded on a 500 MHz Bruker Avance-III spectrometer (Bruker, Daltonics, Bremen, Germany) with TMS as internal standard. Chemical shifts are expressed in δ units; J values for ^1H – ^1H , ^1H – ^{19}F , and ^{13}C – ^{19}F coupling constants are given in Hertz. High-resolution mass spectra (HRMS) were measured using the electrospray ion trap (ESI) technique by collision-induced dissociation on a Bruker APEX-IV (7 Tesla) instrument (Karlsruhe, Germany).

3.1 *N*-methylisatin (**3a**) and 5-fluoro-*N*-methylisatin (**3c**)

These compounds were prepared by *N*-methylation of the appropriate 5-(substituted) isatin with iodomethane according to a reported procedure [18].

3.2 1-Phenylimidazo[1,5-*a*]quinoline (**2**)

This compound was prepared by the reaction of quinoline-2-carbaldehyde (in the presence of iodine, potassium bicarbonate and powdered molecular sieves 4 Å) according to a recently reported procedure [19].

3.3 General procedure for the preparation of 1,3-oxazepino[7,6-*b*]indoles **4a–d** and dihydroacenaphtho[1,2-*f*][1,3]oxazepine **5**

To a stirred solution of DMAD (0.71 g, 5.0 mmol) and substituted isatin or acenaphthoquinone (5.0 mmol) in anhydrous dichloromethane (15 mL) was added dropwise 1-phenylimidazo[1,5-*a*]quinoline (5.0 mmol) in dichloromethane (5 mL) under argon at room temperature. The reaction mixture was stirred for 24 h, the solvent

Table 1: Crystal data and structure refinement for compounds **4c** and **5**.

	4c	5
Empirical formula	C ₃₂ H ₂₄ FN ₃ O ₆	C ₃₅ H ₂₄ N ₂ O ₆ · C ₄ H ₈ O ₂
Formula weight, g mol ⁻¹	565.14	656.66
Temperature, K		293(2)
Radiation/wavelength λ, Å		MoKα/0.71073
Crystal system	Monoclinic	Triclinic
Space group	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> $\bar{1}$
<i>a</i> , Å	16.4069(6)	8.1418(13)
<i>b</i> , Å	10.3131(4)	14.856(3)
<i>c</i> , Å	16.6278(6)	15.6311(18)
α, °	90	115.298(14)
β, °	99.935(3)	100.311(12)
γ, °	90	95.300(14)
Volume, Å ³	2771.33(18)	1651.2(5)
<i>Z</i>	4	2
Density (calcd.), g cm ⁻³	1.3554	1.321
Absorption coefficient μ(MoKα), mm ⁻¹	0.196	0.093
<i>F</i> (000), <i>e</i>	1176.7	688.0
θ range data collection, °	3.18–29.36	5.944–58.712
Index ranges <i>hkl</i>	–20 ≤ <i>h</i> ≤ 13 – 14 ≤ <i>k</i> ≤ 10 –22 ≤ <i>l</i> ≤ 20	–11 ≤ <i>h</i> ≤ 7 –17 ≤ <i>k</i> ≤ 18 –21 ≤ <i>l</i> ≤ 21
Reflections collected	14 810	12 419
Independent reflections/ <i>R</i> _{int} (<i>F</i> ²)	6484/0.0217	7589/0.0445
Refinement method	Full-matrix least-squares on <i>F</i> ²	
Data/restraints/parameters	6484/0/382	7589/0/451
Final <i>R</i> indices <i>R</i> 1 ^a / <i>wR</i> 2 ^b [<i>I</i> > 2 σ(<i>I</i>)]	0.0488/0.1044	0.0915/0.2421
Final <i>R</i> indices <i>R</i> 1 ^a / <i>wR</i> 2 ^b (all data)	0.0846/0.1233	0.1493/0.3209
Goodness-of-Fit ^c on (<i>F</i> ²)	1.009	0.991
Largest diff. peak/hole, e Å ⁻³	0.19/–0.21	0.49/–0.45

^a*R*1 = Σ ||*F*_o – |*F*_c|| / Σ |*F*_o|; ^b*wR*2 = [Σ *w*(*F*_o² – *F*_c²)² / Σ *w*(*F*_o²)²]^{1/2}, *w* = [σ²(*F*_o²) + (*AP*)² + *BP*]⁻¹, where *P* = (Max(*F*_o², 0) + 2*F*_c²)/3; ^cGoF = *S* = [Σ *w*(*F*_o² – *F*_c²)² / (*n*_{obs} – *n*_{param})]^{1/2}.

Table 2: Bond Lengths (Å) and angles (°) for **4c**.

Bond lengths		Bond angles	
O1–C10A	1.3372(19)	C10A–O1–C2	116.61(12)
O1–C2	1.4296(19)	O1–C2–N3	110.58(12)
N3–C2	1.452(2)	O1–C2–C12	111.78(13)
N3–C4	1.423(2)	C19–N3–C2	117.08(14)
C5–C4	1.356(2)	C4–N3–C2	119.86(13)
C5–C5A	1.437(2)	C5–C4–N3	120.51(14)
C10A–C5A	1.400(2)	N3–C4–C27	117.80(14)
C5B–C5A	1.454(2)	C4–C5–C5A	126.55(15)
C5B–C9A	1.410(2)	C5A–C5–C31	115.65(14)
N10–C9A	1.388(2)	C5–C5A–C5B	127.66(14)
N10–C10A	1.342(2)	C10A–C5A–C5	127.73(15)
N10–C36	1.455(2)	C6–C5B–C5A	135.21(15)
C2–C12	1.506(2)	O1–C10A–N10	115.51(14)
N3–C19	1.379(2)	C9–C9A–N10	128.77(16)
C4–C27	1.471(2)	C10A–N10–C36	125.09(15)
C7–F35	1.359(2)	O20–C19–N3	120.52(17)

Table 3: Bond lengths (Å) and angles (°) for **5**.

Bond lengths		Bond angles	
O7–C6B	1.333(4)	C6B–O7–C8	119.1(2)
O7–C8	1.431(3)	O7–C8–N9	111.3(3)
N9–C8	1.461(4)	O7–C8–C13	112.3(2)
N9–C10	1.411(4)	C20–N9–C8	117.2(3)
C10–C11	1.351(5)	C10–N9–C8	116.6(2)
C11A–C11	1.452(4)	C11–C10–N9	118.2(3)
C11A–C6B	1.383(5)	N9–C10–C28	120.9(3)
C11A–C11B	1.500(5)	C10–C11–C11A	123.8(3)
C11C–C11B	1.423(4)	C11A–C11–C32	116.0(3)
C11C–C6A	1.386(5)	C11–C11A–C11B	124.0(3)
C6A–C6	1.379(5)	C6B–C11A–C11	129.2(3)
C13–C8	1.510(4)	C1–C11B–C11A	137.3(3)
C28–C10	1.482(4)	O7–C6B–C6A	117.9(3)
N9–C20	1.376(4)	C6–C6A–C6B	133.8(4)
C6A–C6B	1.456(4)	C1–C11B–C11C	117.3(3)
O21–C20	1.215(4)	C6A–C11C–C11B	111.2(3)

then removed *in vacuo*, the residue soaked in *n*-hexane (10 mL), whereby the desired compound was produced as solid powder; It was then collected by suction filtration, air dried, and purified by chromatographic separation on silica gel plates, eluting with *n*-hexane-ethyl acetate (4:1, *v/v*).

3.3.1 (±)-Dimethyl 3-benzoyl-3,10-dihydro-10-methyl-2-(quinolin-2-yl)-2*H*-oxazepino[7,6-*b*]indolo-4,5-dicarboxylate (4a)

Orange solid; yield: 40%; m.p. 144–145°C. ^1H NMR (500 MHz, CDCl_3): δ = 3.46 (s, 3H, 5- CO_2CH_3), 3.60 (s, 3H, 4- CO_2CH_3), 3.97 (s, 3H, *N*- CH_3), 7.10 (pseudo t, 1H, 7-H), 7.30 (pseudo t, 1H, 8-H), 7.31 (d, J = 6.9 Hz, 1H, 9-H), 7.36 (pseudo t, 2H, 3''-H/5''-H), 7.38 (t, J = 7.2 Hz, 1H, 4''-H), 7.39 (d, J = 8.5 Hz, 1H, 3'-H), 7.44 (d, J = 7.2 Hz, 1H, 6-H), 7.52 (pseudo t, 1H, 6'-H), 7.56 (d, J = 7.2 Hz, 2H, 2''-H/6''-H), 7.57 (pseudo t, 1H, 7'-H), 7.70 (d, J = 8.4 Hz, 1H, 5'-H), 7.72 (d, J = 8.7 Hz, 1H, 8'-H), 8.02 (d, J = 8.5 Hz, 1H, 4'-H), 8.35 (s, 1H, 2-H) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 28.8 (CH_3 -N), 51.6 (5- CO_2CH_3), 52.4 (4- CO_2CH_3), 82.6 (C-2), 90.9 (C-5a), 108.9 (C-9), 117.9 (C-6), 118.7 (C-3'), 119.1 (C-5), 121.9 (C-7), 122.1 (C-8), 123.8 (C-5b), 127.1 (C-5'), 127.4 (C-6'), 127.5 (C-4'a), 128.0 (C-3''/5''), 128.1 (C-2''/6''), 129.6 (C-7'), 129.7 (C-8'), 131.2 (C-4''), 133.4 (C-9a), 135.4 (C-1''), 136.6 (C-4), 137.0 (C-4'), 147.0 (C-8'a), 152.6 (C-2'), 154.1 (C-10a), 163.3 (5- CO_2Me), 166.8 (4- CO_2Me), 171.1 (N-COPh) ppm. – HRMS (ESI): m/z = 548.18348 (calcd. 548.18161 for $\text{C}_{32}\text{H}_{26}\text{N}_3\text{O}_6$, $[\text{M}-\text{H}]^-$).

3.3.2 (±)-Dimethyl 3-benzoyl-3,10-dihydro-7-methoxy-10-methyl-2-(quinolin-2-yl)-2*H*-oxazepino[7,6-*b*]indolo-4,5-dicarboxylate (4b)

Orange solid; yield: 52%; m.p. 124–126°C. ^1H NMR (500 MHz, CDCl_3): δ = 3.41 (s, 3H, 5- CO_2CH_3), 3.62 (s, 3H, 4- CO_2CH_3), 3.77 (s, 3H, 7-O CH_3), 3.84 (s, 3H, *N*- CH_3), 6.84 (d, J = 8.7 Hz, 1H, 8-H), 6.90 (s, 1H, 6-H), 7.17 (d, J = 8.7 Hz, 1H, 9-H), 7.31 (pseudo t, 2H, 3''-H/5''-H), 7.36 (t, J = 7.0 Hz, 1H, 4''-H), 7.38 (d, J = 8.5 Hz, 1H, 3'-H), 7.45 (pseudo t, 1H, 6'-H), 7.52 (d, J = 7.3 Hz, 2H, 2''-H/6''-H), 7.56 (pseudo t, 1H, 7'-H), 7.70 (d, J = 8.0 Hz, 1H, 5'-H), 7.73 (d, J = 8.5 Hz, 1H, 8'-H), 8.03 (d, J = 8.5 Hz, 1H, 4'-H), 8.33 (s, 1H, 2-H) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 28.9 (CH_3 -N), 51.4 (5- CO_2CH_3), 52.4 (4- CO_2CH_3), 55.8 (7-O CH_3), 82.5 (C-2), 91.0 (C-5a), 102.7 (C-6), 109.5 (C-9), 110.5 (C-8), 117.9 (C-3'), 118.7 (C-5), 124.4 (C-5b), 127.1 (C-5'), 127.4 (C-6'), 127.5 (C-9a), 128.0 (C-3''/5''), 128.2 (C-4'a), 128.1 (C-2''/6''), 129.6 (C-8'), 129.7 (C-7'), 131.2 (C-4''),

135.5 (C-1''), 136.5 (C-4), 137.0 (C-4'), 147.0 (C-8'a), 152.6 (C-2'), 154.2 (C-10a), 155.6 (C-7), 163.3 (5- CO_2Me), 166.8 (4- CO_2Me), 171.1 (N-COPh) ppm. – HRMS (ESI): m/z = 548.18348 (calcd. 548.18161 for $\text{C}_{32}\text{H}_{26}\text{N}_3\text{O}_6$, $[\text{M}-\text{H}]^-$).

3.3.3 (±)-Dimethyl 3-benzoyl-3,10-dihydro-7-fluoro-10-methyl-2-(quinolin-2-yl)-2*H*-oxazepino[7,6-*b*]indolo-4,5-dicarboxylate (4c)

Orange crystal; yield: 47%; m.p. 196–198°C. ^1H NMR (500 MHz, CDCl_3): δ = 3.41 (s, 3H, 5- CO_2CH_3), 3.62 (s, 3H, 4- CO_2CH_3), 3.84 (s, 3H, *N*- CH_3), 6.94 (pseudo t, 1H, 8-H), 7.05 (dd, $J_{\text{H-H}}$ = 2.0 Hz, $J_{\text{H-F}}$ = 10.2 Hz, 1H, 6-H), 7.18 (dd, $J_{\text{H-H}}$ = 8.5 Hz, $J_{\text{H-F}}$ = 4.0 Hz, 1H, 9-H), 7.31 (pseudo t, 2H, 3''-H/5''-H), 7.37 (d, J = 8.5 Hz, 1H, 3'-H), 7.39 (t, J = 8.8 Hz, 1H, 4''-H), 7.43 (pseudo t, 1H, 6'-H), 7.52 (pseudo t, 1H, 7'-H), 7.53 (d, J = 6.5 Hz, 2H, 2''-H/6''-H), 7.69 (d, J = 7.9 Hz, 1H, 5'-H), 7.70 (d, J = 8.2 Hz, 1H, 8'-H), 8.03 (d, J = 8.5 Hz, 1H, 4'-H), 8.36 (s, 1H, 2-H) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 29.0 (CH_3 -N), 51.6 (5- CO_2CH_3), 52.4 (4- CO_2CH_3), 82.7 (C-2), 91.0 (C-5a), 105.0 ($^2J_{\text{C-F}}$ = 25.4 Hz, C-6), 109.6 (d, $^3J_{\text{C-F}}$ = 9.7 Hz, C-9), 109.7 ($^2J_{\text{C-F}}$ = 25.5 Hz, C-8), 117.9 (C-3'), 119.3 (C-5), 124.4 ($^3J_{\text{C-F}}$ = 10.1 Hz, C-5b), 127.2 (C-5'), 127.4 (C-6'), 127.5 (C-4'a), 128.0 (C-3''/C-5''), 128.1 (C-2''/C-6''), 129.6 (C-7'), 129.8 (C-8'), 131.0 (C-9a), 131.3 (C-4''), 135.5 (C-1''), 136.1 (C-4), 137.1 (C-4'), 146.9 (C-8'a), 152.3 (C-2'), 154.7 (C-10a), 159.1 ($^1J_{\text{C-F}}$ = 236.4 Hz, C-7), 163.2 (5- CO_2Me), 166.6 (4- CO_2Me), 171.0 (N-COPh) ppm. – HRMS (ESI): m/z = 548.18348 (calcd. 548.18161 for $\text{C}_{32}\text{H}_{26}\text{N}_3\text{O}_6$, $[\text{M}-\text{H}]^-$).

Light-orange needle-like crystals suitable for X-ray crystallography were obtained by allowing a warm solution of **4c** in ethyl acetate-*n*-hexane (1:1, *v/v*) to stand at r. t. for 2–3 days.

3.3.4 (±)-Dimethyl 3-benzoyl-3,10-dihydro-10-phenyl-2-(quinolin-2-yl)-2*H*-oxazepino[7,6-*b*]indolo-4,5-dicarboxylate (4d)

Orange solid; yield: 42%; m.p. 130–132°C. ^1H NMR (500 MHz, CDCl_3): δ = 3.49 (s, 3H, 5- CO_2CH_3), 3.64 (s, 3H, 4- CO_2CH_3), 7.10 (pseudo t, 1H, 7-H), 7.18 (pseudo t, 1H, 8-H), 7.24 (d, J = 8.4 Hz, 1H, 9-H), 7.35 (pseudo t, 2H, 3''-H/4''-H), 7.41 (t, J = 7.2 Hz, 1H, 4''-H), 7.42 (d, J = 8.2 Hz, 1H, 6-H), 7.44 (d, J = 8.4 Hz, 1H, 3'-H), 7.49 (pseudo t, 1H, 6'-H), 7.58 (d, J = 6.5 Hz, 2H, 2''-H/5''-H), 7.59 (pseudo t, 1H, 7'-H), 7.74 (d, J = 7.4 Hz, 1H, 5'-H), 7.78 (d, J = 8.3 Hz, 1H, 8'-H), 8.08 (d, J = 8.4 Hz, 1H, 4'-H), 8.42 (s, 1H, 2-H) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 51.7 (5- CO_2CH_3), 52.5 (4- CO_2CH_3), 82.1 (C-2), 91.5 (C-5a), 110.2 (C-9), 118.0 (C-6), 118.7 (C-3'), 119.8

(C-5), 122.3 (C-8), 122.4 (C-7), 124.0 (C-5b), 126.9 (C-2'''/C-6'''), 127.1 (C-5'), 127.5 (C-6'), 127.6 (C-4'a), 127.6 (C-4'''), 127.8 (C-3''/5''), 128.1 (C-2''/6''), 128.6 (C-3'''/C-5'''), 129.6 (C-7'), 129.7 (C-8'), 131.3 (C-4''), 134.0 (C-9a), 134.9 (C-1'''), 135.4 (C-1''), 136.3 (C-4), 137.1 (C-4'), 146.9 (C-8'a), 152.3 (C-2'), 153.7 (C-10a), 163.3 (5-CO₂Me), 166.8 (4-CO₂Me), 171.0 (N-COPh) ppm. –HRMS (ESI): *m/z* = 60 818 303 (calcd. 60 818 271 for C₃₇H₂₆N₃O₆, [M–H][–]).

3.3.5 Dimethyl 9-benzoyl-8-(quinolin-2-yl)-8,9-dihydroacenaphtho[1,2-*f*][1,3]oxazepine-10,11-dicarboxylate (5)

Orange solid; yield: 34%; m.p. 177–179°C. ¹H NMR (500 MHz, CDCl₃): δ = 3.53 (s, 3H, 5-CO₂CH₃), 3.62 (s, 3H, 4-CO₂CH₃), 7.31 (pseudo t, 2H, 3''-H/5''-H), 7.37 (t, *J* = 7.2 Hz, 1H, 4''-H), 7.42 (pseudo t, 1H, 2-H), 7.43 (pseudo t, 1H, 6'-H), 7.47 (d, *J* = 7.2 Hz, 1H, 1-H), 7.50 (d, *J* = 8.5 Hz, 1H, 3'-H), 7.57 (d, *J* = 7.5 Hz, 2H, 2''-H/6-H''), 7.58 (pseudo t, 1H, 7'-H), 7.69 (d, *J* = 7.9 Hz, 1H, 5'-H), 7.71 (pseudo t, 1H, 5-H), 7.72 (d, *J* = 7.8 Hz, 1H, 8'-H), 7.78 (d, *J* = 8.4 Hz, 1H, 3-H), 7.98 (d, *J* = 8.0 Hz, 1H, 4-H), 8.00 (d, *J* = 8.5 Hz, 1H, 4'-H), 8.12 (d, *J* = 6.9 Hz, 1H, 6-H), 8.44 (s, 1H, 8-H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 51.8 (10-CO₂CH₃), 52.4 (11-CO₂CH₃), 84.6 (C-8), 109.2 (C-11a), 118.6 (C-3'), 122.5 (C-1), 123.3 (C-6), 125.6 (C-3), 126.3 (C-11c), 126.5 (C-11), 127.1 (C-5'), 127.4 (C-6'), 127.5 (C-4'a), 127.9 (C-3''/C-5''), 128.1 (C-2''/C-6''), 128.1 (C-2), 128.3 (C-3a), 129.4 (C-8'), 129.7 (C-5), 130.7 (C-4), 131.2 (C-4''), 132.6 (C-6a), 135.3 (C-11b), 135.8 (C-1''), 136.6 (C-10), 137.2 (C-4'), 153.8 (C-2'), 162.8 (C-6b), 163.0 (11-CO₂Me), 166.4 (10-CO₂Me), 171.6 (N-COPh) ppm. –HRMS (ESI): *m/z* = 567.15499 (calcd. 567.15616 for C₃₅H₂₃N₂O₆, [M–H][–]).

Red needle-like crystals suitable for X-ray crystallography were obtained by allowing a warm solution of **5** in ethyl acetate-*n*-hexane (1:1, *v/v*) to stand at r. t. for 1–2 days.

4 Collection of X-ray diffraction data and structure analysis of compounds **4c** and **5**

Suitable single crystals of **4c** (with approximate dimensions of 0.08 × 0.04 × 0.02 mm³) and **5** with approximate dimensions of 0.08 × 0.06 × 0.02 mm³ were epoxy-mounted on glass fibers. Data for **4c** and **5** were then collected at room temperature (*T* = 293 K) using an Oxford Calibur Diffractometer. Data were acquired and processed to give SHELX-format *hkl* files using CRYSLISPRO software

[20]. Cell parameters were determined and refined using CRYSLISPRO [20]. A multiscan absorption collection was applied with maximum and minimum transmission factors of 1.000 and 0.929, and 1.000 and 0.893 for compounds **4c** and **5**, respectively. The structures were solved by Direct Methods and refined by full-matrix least-squares on *F*² using all unique data [21]. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in calculated positions and refined using a riding model.

CCDC 1917375 and 1952187 contain the supplementary crystallographic data for compounds **4c** and **5**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

5 Supporting information

¹H and ¹³C NMR spectra of representative compounds **4a** (Figs. S1–S11), **4b** (Figs. S12–S23), **4c** (Figs. S24–S34), **4d** (Figs. S35–S46) and **5** (Figs. S47–S58) are given as supplementary material available online (DOI: 10.1515/znb-2019-0150).

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