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Cycloaddition of C,C-Disubstituted Ketonitrones with Acceptor Methylenecyclopropanes and Subsequent Rearrangement Cascade of 5-Spirocyclopropane-isoxazolidines

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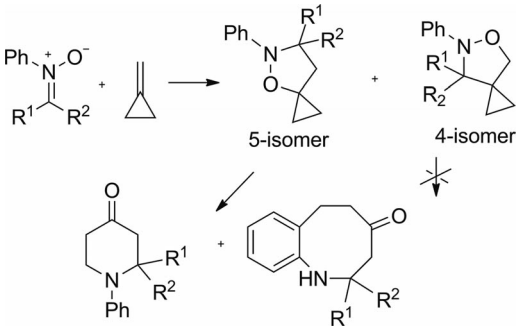
A new reaction cascade to give tricyclic cores of 2,4-dihydro-1*H*-azeto[1,2-*a*]quinolines (benzocarbacephems) and pyrrolo[1,2-*a*]quinolines starting from acyclic *N*-aryl ketonitrones and acceptor ring substituted methylenecyclopropanes has been reported. This reaction includes 1,3-dipolar cycloaddition of *N*-aryl-*C*,*C*-diaryl or *N*-aryl-*C*,*C*-bis(methoxycarbonyl) nitrones **1** to the double bond of dimethyl methylenecyclopropane-1,2-dicarboxylate **2** or benzylidenecyclopropane-1,1-dicarboxylate **3**, followed by Brandi–Guarna rearrangement of the initially formed 5-spirocyclopropane-isoxazolidine cycloadducts to give 2,4-dihydro-1*H*-azeto[1,2-*a*]quinolines **4** or pyrrolo[1,2-*a*]quinolines **6**.

Introduction

Different transformations of methylenecyclopropanes, for instance ring expansion, cycloadditions, and ring-opening reactions have been intensively studied during past decades.[1–4] The release of strain energy in methylenecyclopropanes causes significant enhancement of their reactivity in a number of reactions where simple alkenes (e.g. alkyl-substituted ethylenes) are not active. In many cases initially formed cycloadducts possess high strain energy. This may facilitate subsequent cascade transformations of the initially formed products.[1a,4]

1,3-Dipolar cycloaddition of nitrones to the double carbon–carbon bond of methylenecyclopropanes is one of the most extensively studied cycloaddition reactions of methylenecyclopropanes due to rich chemistry of spirocyclopropane cycloadducts formed in these reactions.[4f,4k,5] In most cases 5-spirocyclopropane-isoxazolidine regioisomers are formed predominantly or exclusively (Scheme 1). 5-Spirocyclopropane-isoxazolidines contain a highly strained spirocyclopropane ring and a comparatively weak adjacent N–O bond that facilitates subsequent Brandi–Guarna rearrangement with the formation of piperidin-4-ones and a number of related products (Scheme 1).[6] Rich chemistry of transformations of 5-spirocyclopropane-isoxazolidines was exploited in the synthesis of different azaheterocycles, e.g. tetrahydropyridones, benzoazocinones, azetidinones.[7]



Scheme 1. Dipolar cycloaddition of nitrones and methylenecyclopropanes.

Regioselectivity of 1,3-dipolar cycloaddition reactions in general is determined by electronic structure of reactants, steric factors or combinations of both.[5,8] It was shown previously that electronic structure of methylenecyclopropanes can be altered by ring substitution with acceptor groups such as carboxylic functions or ester groups. This causes changes of the reactivity of acceptor-substituted cyclopropenes and methylenecyclopropanes in the 1,3-dipolar cycloaddition reactions with carbonyl ylides and nitrones.[9,10] In particular, in reactions between acceptor ring-substituted methylenecylopropanes and *C*,*N*-diarylnitrones thermally stable regioisomeric 4-spirocyclopropane-isoxazolidines are formed[9,10] instead of regioisomeric 5-spirocyclopropane-isoxazolidines observed for unsubstituted or alkyl-substituted methylenecyclopropanes.[4f,4k]

In this paper we report a study of the reaction between *N*,*C*,*C*-trisubstituted nitrones **1** and ring acceptor-substituted dimethyl methylenecyclopropane-1,2-dicarboxylate **2** or arylmethylidenecyclopropane-1,1-dicarboxylates **3a**–**c**.

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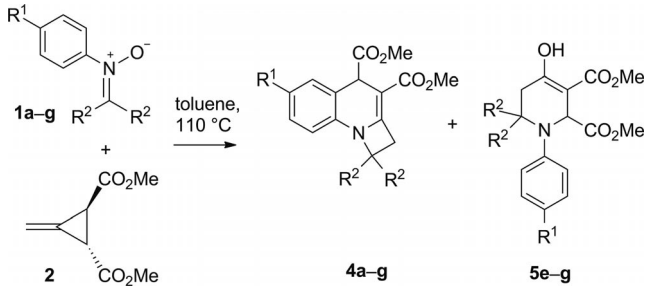
The increased steric hindrance of *N*,*C*,*C*-trisubstituted nitrones causes inversion of the regioselectivity of the 1,3-dipolar cycloaddition reaction with the formation of 5-spirocyclopropane-isoxazolidines. *N*-Aryl-substituted 5-spirocyclopropane-isoxazolidines cannot be isolated and undergo a previously unknown reaction cascade with the formation of products containing tricyclic frameworks of benzocarbacepham and pyrrolo[1,2-*a*]quinolines – structural moieties of antibiotics and biologically active compounds.[11,12]

Results and Discussion

Methylenecyclopropanes **2** and **3** represent vicinal and geminal ring-substituted materials that are easily accessible in gram quantities by known procedures.[13] In initial experiments, ester **2** was heated in toluene at 110 °C for 70–90 hours in the presence of slight excess (1.1 equiv.) of triarylnitrones **1a**–**d**. Azetoquinolines **4a**–**d** were isolated by chromatography on silica gel in modest yields 2–20% (Scheme 2, Table 1). Use of different reaction conditions (temperature, reaction time) did not change yields significantly. The reaction yields are limited by the thermal stability of triarylnitrones. Feist's ester **2** can be recovered from reaction mixtures (up to 70%). The formation of products **4** is surprising since cycloaddition of *C*,*N*-disubstituted nitrones to the same methylenecyclopropanes **2** and **3** give only isomeric 4-spirocyclopropane-isoxazolidines (Scheme 2).[9,10]



Scheme 2. Reaction between nitrones **1a**–**g** and methylenecyclopropane **2**.

Table 1. Reaction scope of the reaction in Scheme 2.

Entry	R^1	R^2	Time [h]	Product	Isolated yield [%]
1	**1a**, H	Ph	91	**4a**	14 (19[a])
2	**1b**, Cl	Ph	80	**4b**	3
3	**1c**, Me	Ph	70	**4c**	20 (41)[a]
4	**1d**, MeO	Ph	77	**4d**	2
5	**1e**, H	CO_2Me	70	**4e**	42
6	**1f**, Cl	CO_2Me	66	**4f**	40
7	**1g**, Me	CO_2Me	74	**4g**	54

[a] Yield based on the recovered ester **2**.

By varying the structure of trisubstituted nitrones we found that more electrophilic ketonitrones **1e**–**g** gave much better yields of the products **4e**–**g** up to 54%. Minor side products **5e**–**g** can also be isolated from crude reaction mixtures (yields 10–16%).

The structure of products **4** were established on the basis of their spectroscopic data and X-ray data for compounds **4c** and **4e** (Figure 1).

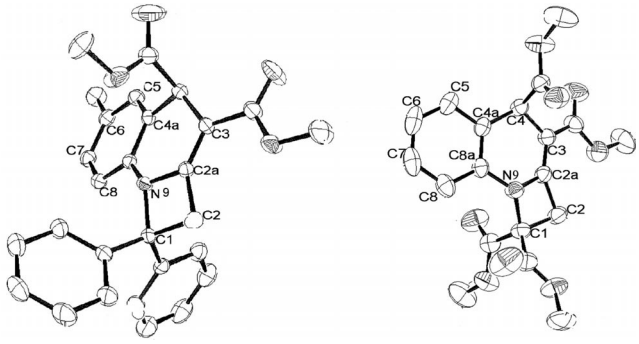
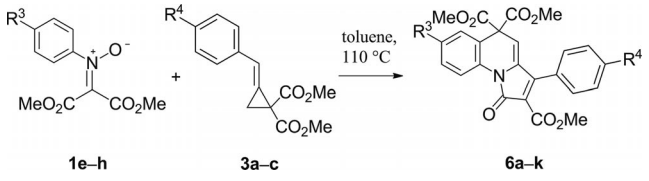


Figure 1. ORTEP diagram for **4c** (left) and **4e** (right). Hydrogen atoms omitted.

Cycloaddition reactions between geminal acceptor substituted methylenecyclopropanes **3a**–**c** and nitrones **1e**–**h** proceed under similar conditions (toluene, 110 °C, 2–5 days until disappearance of starting materials by TLC) with the formation of pyrrolo[1,2-*a*]quinolines **6a**–**d** in good yields of up to 81% (Scheme 3, Table 2). The structure of products **6** were established on the basis of their spectroscopic data and X-ray data for compound **6a** (Figure 2).



Scheme 3. Reaction between nitrones **1e**–**h** and methylenecyclopropane **3a**–**c**.

Table 2. Reaction scope of the reaction in Scheme 3.

Entry	R^3	R^4	Product	Isolated yield [%]
1	H	H	**6a**	81
2	Cl	H	**6b**	66
3	Me	H	**6c**	78
4	MeO	H	**6d**	51
5	H	Me	**6e**	64
6	Cl	Me	**6f**	64
7	Me	Me	**6g**	68
8	MeO	Me	**6h**	32
9	H	Cl	**6i**	67
10	Cl	Cl	**6j**	48
11	Me	Cl	**6k**	43

Previous literature data suggest that the presence of an aryl group at the nitrogen atom of nitrones can play an important role in directing reaction towards formation of eight-membered azocines vs. six-membered tetrahydropyridines.[7] The *N*-methyl-substituted nitrone **7** has been chosen to study the role of the substitution at the nitrogen atom

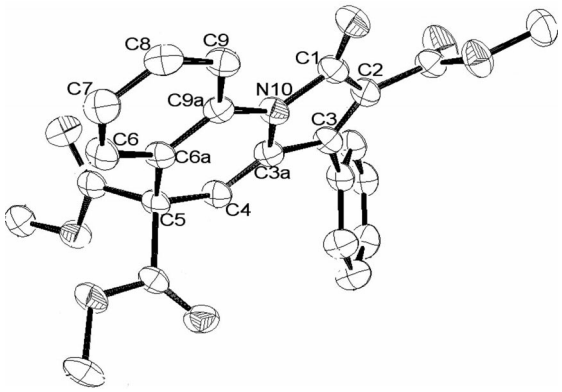
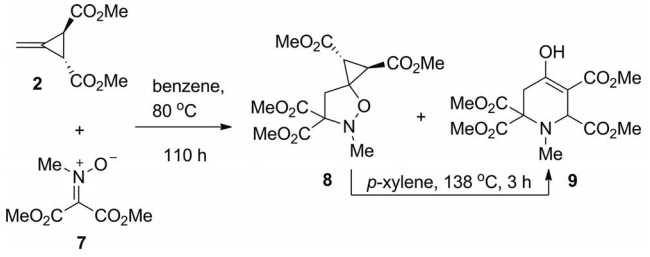


Figure 2. X-ray structure of **6a**. Hydrogen atoms omitted for clarity.

of nitrones on the reaction outcome. The 1,3-dipolar cycloaddition reaction between **7** and Feist's ester **2** (benzene, 80 °C, 4–5 d) leads to the formation of the corresponding 5-spirocyclopropane-isoxazolidine cycloadduct **8** (yield 79%) together with small amounts of **9** (yield 3%) (Scheme 4). Analysis of the crude reaction mixture by ^{1}H NMR spectroscopy does not show the presence of signals of possible 4-spirocyclopropane-isoxazolidine cycloadducts or any other side products. Product **9** can be also obtained by heating cycloadduct **8** in *p*-xylene (Scheme 4). The obtained



Scheme 4. Reaction between nitrone **7** and methylenecyclopropane **2**.

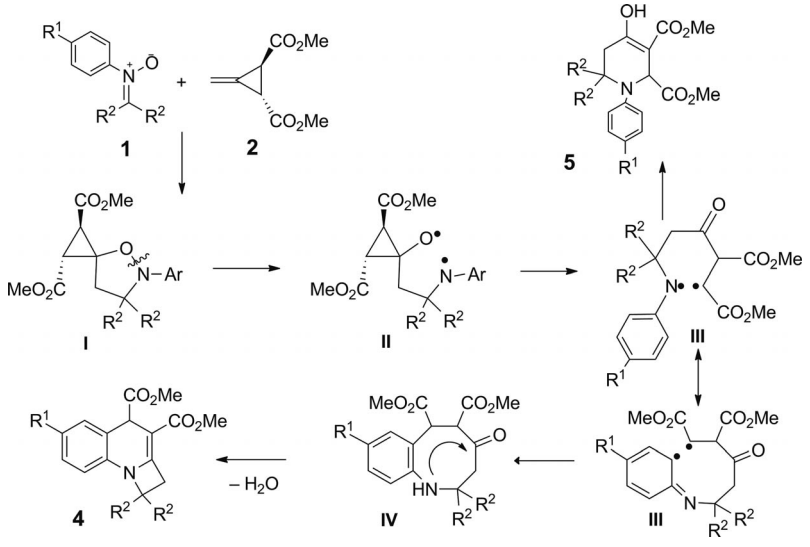
data allows to conclude that the formation of products **4** and **6** is driven by the presence of *N*-aryl substituents since no similar products were observed in the reaction with *N*-methyl nitrone **7**.

In line with literature data, the initial formation of thermally unstable 5-spirocyclopropane-isoxazolidines can be proposed in cycloaddition reactions between methylenecyclopropanes **2**, **3** and nitrones **1**.[4f]

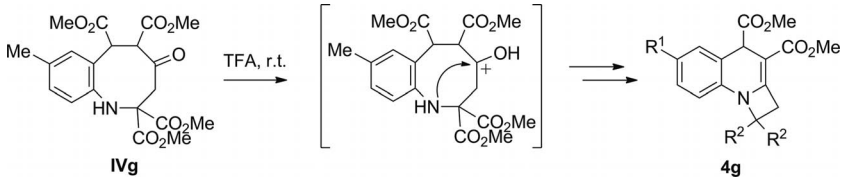
Regioselectivity in the 1,3-dipolar cycloaddition with nitrones can be controlled by frontier molecular orbitals interactions or by use of sterically demanded substrates.[8] The X-ray structure of triphenylnitrone **1a** shows significant out-of-plane rotation of both *C*,*C*-phenyl rings that makes trisubstituted nitrones sterically overcrowded at the carbon atom of a nitrone dipole.[14] Thus, the inversion of the regiochemical results studied for the systems in this paper relative to the previously reported cycloaddition reactions of the same methylenecyclopropanes **2** and **3** can be explained by taking into account steric factors.

The initial slow step in the studied reactions is a "normal" 1,3-dipolar cycloaddition of methylenecyclopropanes with nitrones to form 5-spirocyclopropane-isoxazolidine cycloadducts **I** (Scheme 5). These cycloadducts **I** are thermally unstable and can undergo a thermally induced Brandi–Guarna rearrangement.[6] The biradicals **III** can undergo ring closure to form either six-membered piperidinones **5** or eight-membered azocinones **IV**. For the reaction between **2** and **1g**, the corresponding azocinone intermediate **IVg** can be detected by ^{1}H NMR after heating the reaction mixture for only 10 h.

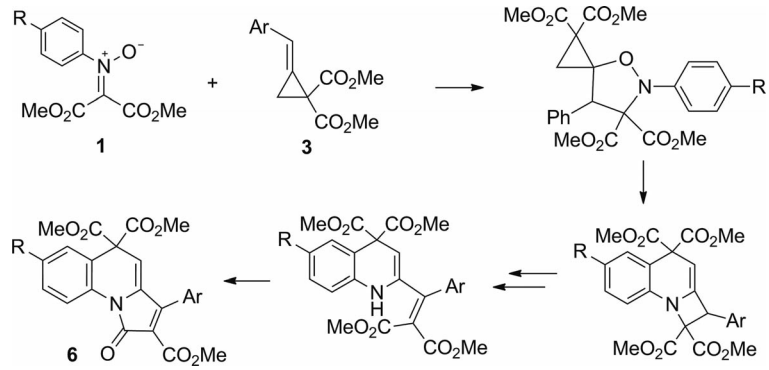
The presence of acceptor ester groups in the eight membered rings of intermediates **IV** may facilitate transannular nucleophilic attack of a lone pair of nitrogen atom to a carbonyl group to form azetoquinolines **4**.[15–17] Note, that azocinone **IVg** undergo complete conversion to **4g** by addition of catalytic amounts of trifluoroacetic acid (Scheme 6).



Scheme 5. Proposed mechanism for the reaction between nitrones **1** and methylenecyclopropane **2**.



Scheme 6. Isomerization of azocinone IVg into azetoquinoline **4g**.



Scheme 7. Proposed mechanism for the reaction between nitrones **1** and methylenecyclopropanes **3**.

Azetoquinolines can also be proposed as intermediates for the reaction of methylenecylopropane **3** with geminal ester groups (Scheme 7). In this case the proposed azetoquinoline intermediates can undergo ring opening and cyclocondensation to give pyrroloquinolines **6**.

Frameworks of both azetoquinolines **4** and pyrroloquinolines **6** are pharmaceutically relevant. Previous examples of the formation of benzocarbacephem cores included different cyclizations of the substituted azetidinones or the use of bicyclic heterocycles for further functionalization.[18] In the current approach, tricyclic benzocarbacephem cores can be obtained in one-pot procedure directly from acyclic nitrones and methylenecyclopropanes. This process can be characterized as rather efficient, taking into account complexity of the described reaction cascade.

Conclusions

Reactions between acceptor ring-substituted methylenecyclopropanes **2** and **3** and trisubstituted *N*,*C*,*C*-triaryl and *N*-aryl-*C*,*C*-bis(methoxycarbonyl)nitrones **1** proceed with the formation of 2,4-dihydro-1*H*-azeto[1,2-*a*]quinolines and pyrrolo[1,2-*a*]quinolines in moderate to good yields. The increased steric demand of trisubstituted nitrones changes regiochemical outcome, so that 5-spirocyclopropane-isoxazolidines are formed or can be postulated as intermediate cycloadducts in the studied reactions. A proposed mechanism for the reaction includes Brandi–Guarna rearrangement of the initially formed cycloadducts followed by transannular cyclization of the intermediate azocinones.

Experimental Section

General: All reactions were performed in anhydrous solvents under an argon atmosphere. Toluene was distilled from Na/benzophenone. Dimethyl methylenecyclopropane-1,2-dicarboxylate **2**, dimethyl 2-benzylidenecyclopropane-1,1-dicarboxylate **3** and nitrones **1** were prepared following known procedures.[13] Reaction progress was monitoring using thin-layer chromatography. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or [D_6]DMSO (300 and 75 MHz accordingly). IR spectra were recorded in 1–5% $CHCl_3$ solutions.

General Procedure: A mixture of methylenecyclopropanedicarboxylate **2** (2 mmol) and the corresponding nitrone **1a**–**g** (1.1 equiv.) was heated at reflux in dry toluene for 66–91 h. The solvent was removed under reduced pressure, and products were isolated by chromatography of the residue on silica gel eluting with petroleum ether/ethyl acetate mixtures followed by crystallization from ethanol.

Dimethyl 1,1-Diphenyl-2,4-dihydro-1*H*-azeto[1,2-*a*]quinoline-3,4-dicarboxylate (4a): Obtained from 510 mg (3 mmol) of the ester **2** and 982 mg (3.6 mmol) of the nitrone **1a**. Yield of **4a** 180 mg (14%). White solid, m.p. 187–189 °C. R_f = 0.53 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3060, 2960, 1730 (s), 1680 (s), 1600, 1490, 1440, 1380, 1310, 1120, 1080 cm^{-1}. ^{1}H NMR ([D_6]DMSO): δ = 3.57 (s, 3 H), 3.64 (s, 3 H), 3.80 (d, J = 16.7 Hz, 1 H), 3.96 (d, J = 16.7 Hz, 1 H), 4.88 (s, 1 H), 6.10–6.13 (m, 1 H), 6.94–7.04 (m, 4 H), 7.30–7.53 (m, 9 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 44.0 (CH), 48.8 (CH_2), 51.4 (CH_3), 52.8 (CH_3), 91.0 (C), 113.6 (CH), 120.6 (C), 123.6 (CH), 127.1 (CH), 128.0 (CH), 128.1 (CH), 128.7 (CH), 128.9 (CH), 129.0 (CH), 130.4 (CH), 136.2 (C), 140.0 (C), 141.9 (C), 156.2 (C), 167.5 (CO), 173.5 (CO) ppm. $C_{27}H_{23}NO_4$ (425.48): calcd. C 76.22, H 5.45, N 3.29; found C 76.09, H 5.48, N 3.10.

Dimethyl 6-Chloro-1,1-diphenyl-2,4-dihydro-1*H*-azeto[1,2-*a*]quinoline-3,4-dicarboxylate (4b): Obtained from 552 mg (3.2 mmol) of the ester **2** and 1.0 g (3.3 mmol) of the nitrone **1b**. Yield of **4b** 39 mg (3%). Yellowish oil. R_f = 0.58 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3055, 2970, 1745 (s), 1690 (s), 1610, 1500, 1455, 1380, 1300, 1110 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.72 (s, 3 H), 3.76 (s, 3 H), 3.88 (d, J = 16.0 Hz, 1 H), 3.98 (d, J = 16.0 Hz, 1 H), 4.95 (s, 1 H), 6.09 (d, J = 8.4 Hz, 1 H), 6.84–6.88 (m, 1 H), 7.11–7.13 (m, 3 H), 7.41–7.47 (m, 8 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 43.9 (CH), 48.7 (CH_2), 51.6

(CH_3), 53.0 (CH_3), 91.0 (C), 114.5 (CH), 122.2 (C), 126.9 (CH), 127.9 (CH), 128.2 (CH), 128.3 (CH), 128.5 (C), 128.9 (CH), 129.0 (CH), 129.1 (CH), 130.3 (CH), 134.9 (C), 139.4 (C), 141.6 (C), 156.2 (C), 167.3 (CO), 173.0 (CO) ppm. HRMS (ESI): Found 941.2357 [2M + Na]$^+$. Calcd. for $C_{27}H_{22}ClNO_4$: 941.2372 [2M + Na]$^+$.

Dimethyl 6-Methyl-1,1-diphenyl-2,4-dihydro-1*H*-azeto[1,2-*a*]quinoline-3,4-dicarboxylate (4c): Obtained from 170 mg (1 mmol) of the ester **2** and 373 mg (1.3 mmol) of the nitrone **1c**. Yield of **4c** 86 mg (20%). White solid, m.p. 183–185 °C. R_f = 0.54 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3050, 2960, 1740 (s), 1670 (s), 1610, 1530, 1450, 1370, 1245, 1095 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.24 (s, 3 H), 3.70 (s, 3 H), 3.75 (s, 3 H), 3.87 (d, J = 16.0 Hz, 1 H), 3.96 (d, J = 16.0 Hz, 1 H), 4.95 (s, 1 H), 6.07 (d, J = 8.0 Hz, 1 H), 6.70–6.72 (m, 1 H), 7.13–7.47 (m, 11 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2 (CH_3), 44.1 (CH), 48.9 (CH_2), 51.3 (CH_3), 52.8 (CH_3), 90.5 (C), 113.4 (CH), 120.6 (C), 127.1 (CH), 127.9 (CH), 128.1 (CH), 128.6 (CH), 128.7 (CH), 128.9 (CH), 129.0 (CH), 130.9 (CH), 133.2 (C), 133.7 (C), 139.9 (C), 142.0 (C), 156.2 (C), 167.6 (CO), 173.7 (CO) ppm. $C_{28}H_{25}NO_4$ (439.51): calcd. C 76.52, H 5.73, N 3.19; found C 76.58, H 5.73, N 3.00.

Some crystallographic data for compound **4c**: Colorless crystals, $C_{28}H_{25}NO_4$, M = 439.49, monoclinic, space group $P2_1/c$, a = 11.4824(11), b = 8.6216(9), c = 23.963(3) Å, β = 103.020(2), V = 2311.3(4) Å^3, Z = 4, T = 293 K. Selected bond lengths and angles: C^1–N^9 1.4969(15), C^1–C^2 1.5503(9), C^2–C^{2a} 1.5308(9),C^{2a}–C^3 1.3346(16), C^{2a}–N^9 1.3665(16), N^9–C^1–C^2 86.50, C^{2a}–C^2–C^1 86.37, N^9–C^{2a}–C^2 92.06, C^{2a}–N^9–C^1 94.74.

Dimethyl 6-Methoxy-1,1-diphenyl-2,4-dihydro-1*H*-azeto[1,2-*a*]quinoline-3,4-dicarboxylate (4d): Obtained from 255 mg (1.5 mmol) the ester **2** and 591 mg (1.9 mmol) of the nitrone **1d**. Yield of **4d** 14 mg (2%). Yellowish oil. R_f = 0.38 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3055, 2942, 1740 (s), 1672 (s), 1610, 1510, 1450, 1380, 1270, 1093 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.71 (s, 3 H), 3.73 (s, 3 H), 3.75 (s, 3 H), 3.87 (d, J = 16.0 Hz, 1 H), 3.96 (d, J = 16.0 Hz, 1 H), 4.88 (s, 1 H), 6.12 (d, J = 8.7 Hz, 1 H), 6.47 (dd, J = 16.0, 2.9 Hz, 1 H), 7.00 (d, J = 2.9 Hz, 1 H), 7.12–7.45 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 44.4 (CH), 48.9 (CH_2), 51.4 (CH_3), 52.9 (CH_3), 55.9 (CH_3), 89.6 (C), 113.6 (CH), 114.5 (CH), 115.8 (CH), 122.0 (C), 127.1 (CH), 127.9 (CH), 128.1 (CH), 128.9 (CH), 129.0 (CH), 129.9 (C), 139.9 (C), 142.0 (C), 156.2 (C), 173.5 (CO) ppm. HRMS (ESI): found 933.3325 [2M + Na]$^+$; Calcd. for $C_{28}H_{25}NO_5$: 933.3363 [2M + Na]$^+$.

Tetramethyl 2*H*-Azeto[1,2-*a*]quinoline-1,1,3,4(4*H*)-tetracarboxylate (4e) and Tetramethyl 4-hydroxy-1-phenyl-1,2-dihydro-1*H*-pyridine-2,2,5,6-tetracarboxylate (5e): Obtained from 340 mg (2 mmol) of the ester **2** and 616 mg (2.6 mmol) of the nitrone **1e**. Yield of **4e** 327 mg (42%). White solid, m.p. 127–128 °C. R_f = 0.25 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3060, 2970, 1752 (s), 1702 (s), 1620, 1505, 1451, 1385, 1330, 1312, 1280, 1160, 1140, 1090 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO): δ = 3.57 (s, 3 H), 3.64 (s, 3 H), 3.68 (s, 3 H), 3.73 (d, J = 16.0 Hz, 1 H), 3.86 (s, 3 H), 3.93 (d, J = 16.0 Hz, 1 H), 4.82 (s, 1 H), 6.80 (d, J = 8.0 Hz, 1 H), 7.08 (m, 1 H), 7.25 (m, 1 H), 7.39 (d, J = 7.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 39.0 (CH_2), 43.7 (CH), 51.6 (CH_3), 52.9 (CH_3), 53.8 (CH_3), 53.9 (CH_3), 73.1 (C), 93.5 (C), 113.3 (CH), 120.0 (C), 124.6 (CH), 128.6 (CH), 130.5 (CH), 135.8 (C), 154.2 (C), 166.8 (CO), 167.1 (CO), 167.7 (CO), 173.0 (CO) ppm. $C_{19}H_{19}NO_8$ (389.36): calcd. C 58.61, H 4.92, N 3.60; found C 58.65, H 4.92, N 3.60.

Product 5e: Yield 81 mg (10%). White solid, m.p. 134–135 °C. R_f = 0.30 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3475 (broad), 3060, 2970, 1750 (s), 1682 (s), 1640, 1610, 1510, 1460, 1375, 1320, 1285, 1195, 1100, 1080 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.06 (d, J = 16.7 Hz, 1 H), 3.47 (s, 3 H), 3.52 (s, 3 H), 3.60 (d, J = 16.7 Hz, 1 H), 3.71 (s, 3 H), 3.77 (s, 3 H), 5.23 (s, 1 H), 7.12 (m, 1 H), 7.24–7.34 (m, 4 H), 12.17 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 38.2 (CH_2), 52.3 (CH_3), 52.5 (CH_3), 53.3 (CH_3), 53.4 (CH_3), 60.9 (CH), 71.9 (C), 97.3 (C), 125.8 (CH), 126.9 (CH), 129.1 (CH), 146.2 (C), 168.5 (C), 170.0 (C), 170.3 (C), 170.5 (C), 172.3 (C) ppm. $C_{19}H_{21}NO_9$ (407.37): calcd. C 56.02, H 5.20, N 3.44; found C 56.09, H 5.23, N 3.53.

Tetramethyl 6-Chloro-2*H*-azeto[1,2-*a*]quinoline-1,1,3,4(4*H*)-tetracarboxylate (4f) and Tetramethyl 1-(4-Chlorophenyl)-4-hydroxy-1,2-dihydro-1*H*-pyridine-2,2,5,6-tetracarboxylate (5f): Obtained from 340 mg (2 mmol) of the ester **2** and 706 mg (2.6 mmol) of the nitrone **1f**. Yield of **4f** 340 mg (40%). White solid, m.p. 154 °C. R_f = 0.28 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3060, 2970, 1750 (s), 1710 (s), 1610, 1500, 1452, 1380, 1300, 1160, 1140, 1110, 1090 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.65 (d, J = 16.0 Hz, 1 H), 3.71 (s, 3 H), 3.74 (s, 3 H), 3.77 (s, 3 H), 3.92 (d, J = 16.0 Hz, 1 H), 3.93 (s, 3 H), 4.85 (s, 1 H), 6.87 (d, J = 9.1 Hz, 1 H), 7.16 (dd, J = 9.1, 2.2 Hz, 1 H), 7.41 (d, J = 2.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 39.0 (CH_2), 43.6 (CH), 51.7 (CH_3), 53.1 (CH_3), 53.9 (CH_3), 54.0 (CH_3), 73.2 (C), 93.6 (C), 114.6 (CH), 121.7 (C), 128.7 (CH), 129.5 (C), 130.4 (CH), 134.6 (C), 153.8 (C), 166.5 (CO), 166.9 (CO), 167.5 (CO), 172.5 (CO) ppm. $C_{19}H_{18}ClNO_8$ (423.81): calcd. C 53.85, H 4.28, N 3.31; found C 53.99, H 4.07, N 3.39.

Product 5f: Yield 130 mg (15%). White solid, m.p. 116–117 °C. R_f = 0.33 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3480 (br.), 3060, 2970, 1750 (s), 1682 (s), 1640, 1615, 1510, 1460, 1372, 1320, 1285, 1195, 1100, 1070 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.04 (d, J = 16.7 Hz, 1 H), 3.50 (s, 3 H), 3.52 (s, 3 H), 3.56 (d, J = 16.7 Hz, 1 H), 3.70 (s, 3 H), 3.76 (s, 3 H), 5.15 (s, 1 H), 7.22 (d, J = 9.0 Hz, 2 H), 7.29 (d, J = 9.0 Hz, 2 H), 12.15 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 38.1 (CH_2), 52.3 (CH_3), 52.6 (CH_3), 53.4 (CH_3), 53.5 (CH_3), 60.9 (CH), 71.9 (C), 97.0 (C), 128.5 (CH), 129.2 (CH), 131.3 (C), 144.7 (C), 168.3 (C), 169.8 (C), 170.1 (C), 170.3 (C), 172.0 (C) ppm. $C_{19}H_{20}ClNO_9$ (441.82): calcd. C 51.65, H 4.56, N 3.17; found C 52.07, H 4.45, N 3.29.

Tetramethyl 6-Methyl-2*H*-azeto[1,2-*a*]quinoline-1,1,3,4(4*H*)-tetracarboxylate (4g) and Tetramethyl 4-Hydroxy-1-(4-methylphenyl)-1,2-dihydro-1*H*-pyridine-2,2,5,6-tetracarboxylate (5g): Obtained from 340 mg (2 mmol) of the ester **2** and 653 mg (2.6 mmol) of the nitrone **1g**. Yield of **4g** 430 mg (54%). White solid, m.p. 144–145 °C. R_f = 0.26 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3050, 2970, 1750 (s), 1700 (s), 1628, 1520, 1450, 1380, 1310, 1270, 1165, 1140, 1100 cm^{-1}. ^{1}H NMR (C_6D_6): δ = 2.08 (s, 3 H), 3.15 (s, 3 H), 3.34 (s, 3 H), 3.39 (s, 3 H), 3.56 (s, 3 H), 3.68 (d, J = 16.0 Hz, 1 H), 3.81 (d, J = 16.0 Hz, 1 H), 5.30 (s, 1 H), 6.89 (dd, J = 8.0, 1.5 Hz, 1 H), 7.24 (d, J = 8.0 Hz, 1 H), 7.37 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.3 (CH_3), 39.0 (CH_2), 43.7 (CH), 51.5 (CH_3), 52.9 (CH_3), 53.8 (CH_3), 53.9 (CH_3), 73.0 (C), 93.2 (C), 113.2 (CH), 119.9 (C), 129.2 (CH), 130.8 (CH), 133.4 (C), 134.2 (C), 154.2 (C), 166.9 (CO), 167.2 (CO), 167.8 (CO), 173.2 (CO) ppm. $C_{20}H_{21}NO_8$ (403.39): calcd. C 59.55, H 5.25, N 3.47; found C 59.88, H 5.23, N 3.73.

Product 5g: Yield 130 mg (16%). White solid, m.p. 97–99 °C. R_f = 0.32 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3480 (br.), 3055, 2970, 1750 (s), 1683 (s), 1635, 1530, 1460, 1320, 1280, 1190, 1100, 1072 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.29 (s, 3 H), 3.03 (d, J = 17.0 Hz, 1 H), 3.45 (s, 3 H), 3.50 (s, 3 H), 3.57 (d, J = 17.0 Hz, 1 H), 3.70 (s, 3 H), 3.75 (s, 3 H), 5.19 (s, 1 H), 7.06 (d, J = 8.0 Hz, 2 H), 7.26 (d, J = 8.0 Hz, 2 H), 12.18 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.4 (CH_3), 38.1 (CH_2), 52.3 (CH_3), 52.5 (CH_3), 53.3 (CH_3), 54.0 (CH_3),

61.2 (CH), 72.0 (C), 97.2 (C), 127.9 (CH), 129.7 (CH), 136.0 (C), 143.3 (C), 168.4 (C), 170.1 (C), 170.2 (C), 170.5 (C), 172.3 (C) ppm. $C_{20}H_{23}NO_9$ (421.40): calcd. C 57.00, H 5.50, N 3.32; found C 57.28, H 5.46, N 3.66.

Trimethyl 1-Oxo-3-phenyl-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6a): Obtained from 246 mg (1.0 mmol) of the ester **3** and 261 mg (1.1 mmol) of the nitrone **1e**, time 130 h, yield of **6a** 350 mg (81%). Yellow solid, m.p. 158–159 °C. R_f = 0.31 (EtOAc/hexane = 1:2). IR: ṽ = 3058, 2970, 1750 (s), 1725 (s), 1620, 1510, 1480, 1450, 1380, 1285, 1190, 1165, 1050 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.79 (s, 6 H), 3.82 (s, 3 H), 5.96 (s, 1 H), 7.24 (m, 1 H), 7.44–7.54 (6 H), 7.65 (d, J = 8.6 Hz, 1 H), 8.94 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 52.8 (CH_3), 54.2 (2CH_3), 58.9 (C), 112.0 (CH), 117.5 (CH), 117.9 (C), 125.0 (CH), 128.9 (CH), 129.4 (C), 129.8 (CH), 130.4 (CH), 130.6 (CH), 130.7 (CH), 133.8 (C), 137.0 (C), 149.9 (C), 162.8 (CO), 163.6 (CO), 169.1 (CO) ppm. $C_{24}H_{19}NO_7$ (433.42): calcd. C 66.51, H 4.42, N 3.23; found C 66.53, H 4.30, N 3.32.

Trimethyl 7-Chloro-1-oxo-3-phenyl-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6b): Obtained from 246 mg (1.0 mmol) of the ester **3** and 299 mg (1.1 mmol) of the nitrone **1f**, time 117 h, yield of **6b** 300 mg (64%). Yellow solid, m.p. 177–178 °C. R_f = 0.37 (EtOAc/hexane = 1:2). IR: ṽ = 3042, 2990, 1750 (s), 1720 (s), 1630, 1505, 1450, 1380, 1280, 1185, 1165, 1060 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.81 (s, 6 H), 3.82 (s, 3 H), 5.94 (s, 1 H), 7.43 (dd, J = 7.3, 7.5 Hz, 1 H), 7.47–7.50 (2 H), 7.52–7.56 (3 H), 7.64 (d, J = 2.9 Hz, 1 H), 8.90 (d, J = 8.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 52.9 (CH_3), 54.5 (2CH_3), 58.8 (C), 111.6 (CH), 118.8 (CH), 119.5 (C), 125.0 (C), 129.0 (CH), 129.2 (C), 129.8 (CH), 130.2 (C), 130.5 (CH), 130.6 (CH), 130.8 (CH), 132.4 (C), 136.8 (C), 150.0 (C), 162.6 (CO), 163.5 (CO), 168.6 (CO) ppm. $C_{24}H_{18}ClNO_7$ (467.86): calcd. C 61.61, H 3.88, N 2.99; found C 61.63, H 3.66, N 3.08.

Trimethyl 7-Methyl-1-oxo-3-phenyl-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6c): Obtained from 246 mg (1.0 mmol) of the ester **3** and 276 mg (1.1 mmol) of the nitrone **1g**, time 130 h, yield of **6c** 350 mg (78%). Yellow solid, m.p. 175–177 °C. R_f = 0.31 (EtOAc/hexane = 1:2). IR: ṽ = 3060, 2970, 1747 (s), 1720 (s), 1630, 1520, 1450, 1380, 1270, 1200, 1165, 1060 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.38 (s, 3 H), 3.81 (s, 6 H), 3.82 (s, 3 H), 5.94 (s, 1 H), 7.27 (dd, J = 8.7, 1.5 Hz, 1 H), 7.42 (d, J = 1.5 Hz, 1 H), 7.47–7.55 (5 H), 8.81 (d, J = 8.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.5 (CH_3), 52.8 (CH_3), 54.2 (2CH_3), 58.9 (C), 111.9 (CH), 117.4 (CH), 117.7 (C), 125.0 (C), 128.9 (CH), 129.5 (C), 129.8 (CH), 130.6 (CH), 131.2 (CH), 131.5 (C), 134.6 (C), 137.1 (C), 149.8 (C), 162.9 (CO), 163.4 (CO), 169.2 (CO) ppm. $C_{25}H_{21}NO_7$ (447.44): calcd. C 67.11, H 4.73, N 3.13; found C 67.39, H 4.64, N 3.37.

Trimethyl 7-Methoxy-1-oxo-3-phenyl-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6d): Obtained from 246 mg (1.0 mmol) of the ester **3** and 276 mg (1.1 mmol) of the nitrone **1h**, time 50 h, yield of **6d** 235 mg (51%). Yellow solid, m.p. 153–154 °C. R_f = 0.23 (EtOAc/hexane = 1:2). IR: ṽ = 3055, 2970, 1745 (s), 1715 (s), 1690, 1630, 1517, 1448, 1380, 1290, 1270, 1200, 1160, 1100, 1070 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.77 (s, 6 H), 3.80 (s, 3 H), 3.83(s, 3 H), 5.90 (s, 1 H), 7.00 (dd, 1 H, J = 8.7, 2.9 Hz), 7.16 (d, 1 H, J = 2.9 Hz), 7.46–7.53 (5 H), 8.86 (d, 1 H, J = 8.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ = 52.8 (CH_3), 54.2 (2CH_3), 55.9 (CH_3), 59.1 (C), 111.5 (CH), 115.7 (CH), 115.8 (CH), 118.7 (CH), 119.2 (C), 124.9 (C), 127.6 (C), 128.9 (CH), 129.5 (C), 129.8 (CH), 130.6 (CH), 137.1 (C), 149.6 (C), 156.4 (C), 162.9 (CO), 163.3 (CO), 169.0 (CO) ppm. $C_{25}H_{21}NO_7$ (447.44): calcd. C 64.79, H 4.57, N 3.02; found C 64.77, H 4.35, N 3.18.

Trimethyl 1-Oxo-3-(4-tolyl)-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6e): Obtained from 260 mg (1.0 mmol) of the ester **3b** and 240 mg (1.0 mmol) of the nitrone **1e**, time 100 h, yield of **6e** 288 mg (64%). Yellow solid, m.p. 166 °C. R_f = 0.28 (EtOAc/hexane = 1:2). IR: ṽ = 3034, 2954, 1745 (s), 1723 (s), 1493, 1434, 1363, 1270, 1144, 1055 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.45 (s,3 H), 3.79 (s, 6 H), 3.83 (s, 3 H), 5.98 (s, 1 H), 7.20–7.50 (m, 6 H), 7.64 (d, J = 6.5 Hz, 1 H), 8.93 (d, J = 8.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.9 (CH_3), 52.8 (OCH_3), 54.2 (2OCH_3), 58.9 (C), 111.8 (CH), 117.5 (CH), 117.9 (C), 124.5 (C), 124.9 (CH), 126.5 (C), 129.8 (2CH), 130.4 (CH), 130.5 (CH), 133.9 (C), 137.1 (C), 141.1 (C), 150.1 (C), 163.0 (CO), 163.7 (CO), 169.1 (2CO) ppm. $C_{25}H_{21}NO_7$ (447.44): calcd. C 67.11, H 4.73, N 3.13; found C 67.47, H 4.38, N 3.19.

Trimethyl 7-Chloro-1-oxo-3-(4-tolyl)-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6f): Obtained from 260 mg (1.0 mmol) of the ester **3b** and 300 mg (1.1 mmol) of the nitrone **1f**, time 88 h, yield of **6f** 310 mg (64%). Yellow solid, m.p. 205–206 °C. R_f = 0.27 (EtOAc/hexane = 1:2). IR: ṽ = 3030, 2950, 1742 (s), 1720 (s), 1490, 1438, 1365, 1274, 1140, 1050 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.46 (s,3 H), 3.81 (s, 6 H), 3.83 (s, 3 H), 5.93 (s, 1 H), 7.33 (d, J = 8.0 Hz, 2 H), 7.39 (d, J = 8.0 Hz, 2 H), 7.39 (d, J = 8.0 Hz, 2 H), 7.43 (dd, J = 9.4, 2.1 Hz, 1 H), 7.63 (d, J = 2.1 Hz, 1 H), 8.90 (d, J = 9.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.9 (CH_3), 52.8 (OCH_3), 52.4 (2 OCH_3), 58.8 (C), 111.4 (CH), 118.8 (CH), 119.5 (C), 124.5 (C), 126.3 (C), 129.7 (CH), 129.8 (CH), 130.1 (C), 130.4 (CH), 130.5 (CH), 132.5 (C), 136.8 (C), 141.3 (C), 150.2 (C), 162.8 (CO), 163.6 (CO), 168.7 (2 CO) ppm. $C_{25}H_{20}ClNO_7$ (481.89): calcd. C 62.31, H 4.18, N 2.91; found C 62.16, H 4.30, N 2.84.

Trimethyl 1-Oxo-3,7-bis(4-tolyl)-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6g): Obtained from 260 mg (1.0 mmol) of the ester **3b** and 276 mg (1.1 mmol) of the nitrone **1g**, time 100 h, yield of **6g** 315 mg (68%). Yellow solid, m.p. 193–194 °C. R_f = 0.20 (EtOAc/hexane = 1:3). IR: ṽ = 3030, 2950, 1745 (s), 1727 (s), 1490, 1430, 1360, 1275, 1140, 1060 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.37 (s, 3 H), 2.46 (s, 3 H), 3.79 (s, 6 H), 3.83 (s, 3 H), 5.95 (s, 1 H), 7.25 (d, J = 1.5 Hz, 1 H), 7.33 (d, J = 8.0 Hz, 2 H), 7.39 (d, J = 8.0 Hz, 2 H), 7.40 (m, 1 H), 8.80 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.5 (CH_3), 21.9 (CH_3), 52.7 (OCH_3), 54.2 (2 OCH_3), 58.9 (C), 111.7 (CH), 117.7 (C), 124.5 (C), 126.5 (C), 129.7 (CH), 129.8 (CH), 130.6 (C), 131.2 (CH), 131.5 (C), 134.6 (C), 137.1 (C), 141.0 (C), 149.9 (C), 163.6 (CO), 169.2 (2*CO) ppm. $C_{26}H_{23}NO_7$ (461.47): calcd. C 67.67, H 5.02, N 3.04; found C 67.48, H 5.03, N 3.17.

Trimethyl 7-Methoxy-1-oxo-3-(4-tolyl)-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6h): Obtained from 260 mg (1.0 mmol) of the ester **3b** and 277 mg (1.0 mmol) of the nitrone **1h**, time 90 h, yield of **6h** 155 mg (32%). Yellow solid, m.p. 215 °C (dec.). R_f = 0.22 (EtOAc/hexane = 1:2). IR: ṽ = 3007, 2958, 1748 (s), 1723 (s), 1503, 1436, 1366, 1280, 1144, 1086, 1052, 1029 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.46 (s, 3 H), 3.79 (s, 3 H), 3.83 (s, 3 H), 3.84 (s, 3 H), 5.93 (s, 1 H), 7.02 (dd, J = 9.2, 2.6 Hz, 1 H), 7.18 (d, J = 2.6 Hz, 1 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.39 (d, J = 8.0 Hz, 2 H), 8.87 (d, J = 9.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.9 (CH_3), 52.7 (OCH_3), 54.2 (2 OCH_3), 55.5 (OCH_3), 59.1 (C), 111.3 (CH), 115.7 (CH), 118.7 (CH), 124.5 (C), 126.5 (C), 127.7 (C), 129.6 (CH), 129.8 (CH), 137.1 (C), 140.9 (C), 156.4 (CO), 163.0 (CO), 163.4 (CO), 169.0 (2 CO) ppm. $C_{26}H_{23}NO_8$ (477.47): calcd. C 65.40, H 4.86, N 2.93; found C 65.68, H 5.04, N 3.16.

Trimethyl 3-(4-Chlorophenyl)-1-oxo-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6i): Obtained from 260 mg (1.0 mmol) of the ester **3c** and 240 mg (1.0 mmol) of the nitrone **1e**, time 120 h, yield of **6i** 315 mg (67%). Yellow solid, m.p. 197 °C. R_f = 0.22 (EtOAc/hexane = 1:2). IR: ṽ = 2954, 1749 (s), 1740 (s), 1504, 1437, 1369,

1231, 1144, 1037 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 3.80 (s, 6 H), 3.84 (s, 3 H), 5.92 (s, 1 H), 7.20–7.30 (m, 1 H), 7.40–7.50 (m, 5 H), 7.65 (dd, J = 8.0, 2.4 Hz, 1 H), 8.92 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.5 (CH_3), 52.9 (OCH_3), 54.2 (2 OCH_3), 58.9 (C), 112.0 (CH), 117.4 (CH), 117.6 (C), 125.1 (C), 127.8 (C), 129.3 (CH), 130.7 (CH), 131.2 (2 CH), 131.3 (C), 134.8 (C), 136.9 (C), 137.0 (C), 148.8 (C), 162.7 (2 CO), 163.1 (CO), 169.0 (2 CO) ppm. $C_{25}H_{21}NO_7$ (447.44): calcd. C 67.11, H 4.73, N 3.13; found C 67.47, H 4.38, N 3.19.

Trimethyl 3,7-Dichloro-1-oxo-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6j): Obtained from 260 mg (1.0 mmol) of the ester **3c** and 300 mg (1.1 mmol) of the nitrone **1f**, time 90 h, yield of **6j** 208 mg (43%). Yellow solid, m.p. 222 °C. R_f = 0.24 (EtOAc/hexane = 1:3). IR: $\tilde{\nu}$ = 3031, 2952, 1759 (s), 1745 (s), 1491, 1437, 1369, 1245, 1144, 1037 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 3.81 (s, 6 H), 3.83 (s, 3 H), 5.90 (s, 1 H), 7.44 (m, 1 H), 7.44 (d, J = 7.0 Hz, 2 H), 7.52 (d, J = 7.0 Hz, 2 H), 7.64 (d, J = 2.2 Hz, 1 H), 8.89 (d, J = 9.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 52.9 (OCH_3), 54.5 (2 OCH_3), 58.7 (C), 111.6 (CH), 118.8 (CH), 119.4 (C), 125.1 (C), 127.5 (C), 129.4 (CH), 130.3 (C), 130.5 (CH), 130.6 (CH), 131.2 (CH), 132.3 (C), 136.6 (C), 137.2 (C), 149.1 (C), 162.4 (CO), 163.2 (CO), 168.5 (2*CO) ppm. $C_{24}H_{17}Cl_2NO_7$ (502.31): calcd. C 57.39, H 3.41, N 2.79; found C 57.58, H 3.30, N 2.87.

Trimethyl 3-(4-Chlorophenyl)-7-(4-tolyl)-1-oxo-1*H*-pyrrolo[1,2-*a*]quinoline-2,5,5-tricarboxylate (6k): Obtained from 260 mg (1.0 mmol) of the ester **3c** and 276 mg (1.1 mmol) of the nitrone **1g**, time 90 h, yield of **6f** 207 mg (43%). Yellow solid, m.p. 168 °C. R_f = 0.30 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 2954, 1749 (s), 1740 (s), 1504, 1437, 1369, 1231, 1144, 1039 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 2.38 (s,3 H), 3.80 (s, 6 H), 3.84 (s, 3 H), 5.89 (s, 1 H), 7.27 (d, J = 8.0 Hz, 1 H), 7.40–7.55 (m, 5 H), 8.77 (d, J = 8.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.5 (CH_3), 52.9 (OCH_3), 54.2 (2*OCH_3), 58.9 (C), 112.0 (CH), 117.4 (CH), 117.6 (C), 125.1 (C), 127.8 (C), 129.3 (CH), 130.7 (CH), 131.2 (2*CH), 131.3 (C), 134.8 (C), 136.9 (C), 137.0 (C), 148.8 (C), 162.7 (CO), 163.1 (CO), 169. (2*CO) ppm. $C_{25}H_{20}ClNO_7$ (481.89): calcd. C 62.31, H 4.18, N 2.91; found C 62.16, H 4.30, N 2.84.

Tetramethyl 5-Methyl-4-oxa-5-azaspiro[2.4]heptan-1,2,6,6-tetracarboxylate (8) and Tetramethyl 4-Hydroxy-1-methyl-3,6-dihydro-1*H*-pyridine-2,2,5,6-tetracarboxylate (9): Obtained from 1 mmol (170 mg) of the ester **2** and 1.1 mmol (192 mg) nitrone **7** refluxing in 4 mL of benzene during 106 h. Benzene was evaporated and residue was separated on silica gel (eluent: ethyl acetate/hexane = 1:2), the product was crystallized from ethanol. Yield of **8** 272 mg (79%). White solid, m.p. 100–101 °C. R_f = 0.39 (EtOAc/hexane = 1:1). IR (KBr): $\tilde{\nu}$ = 2956, 1760 (s), 1729 (s), 1614, 1437, 1340, 1274, 1233, 1202, 1148 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 2.46 (d, J = 6.5 Hz, 1 H), 2.81 (s, 3 H), 2.86 (d, J = 6.5 Hz, 1 H), 3.03 (d, J = 14.5 Hz, 1 H), 3.10 (d, J = 14.5 Hz, 1 H), 3.73 (s, 3 H), 3.74 (s, 3 H), 3.80 (s, 3 H), 3.82 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 30.1 (CH), 32.7 (CH), 41.0 (CH_2), 41.3 (CH_3), 52.7 (CH_3), 52.8 (CH_3), 53.4 ($2CH_3$), 70.7 (C), 76.9 (C), 167.4 (CO), 167.6 (CO), 167.7 (CO), 170.1 (CO) ppm. $C_{14}H_{19}NO_9$ (345.31): calcd. C 48.70, H 5.55, N 4.06; found C 48.95, H 5.66, N 4.26.

Product 9: Yield 10 mg (3%). White solid, m.p. 103–104 °C. R_f = 0.34 (EtOAc/hexane = 1:2). IR: $\tilde{\nu}$ = 3470 (broad), 2973, 1740 (s), 1678 (s), 1638 (s), 1610, 1450, 1440, 1307, 1275, 1250, 1180, 1110 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 2.68 (s, 3 H), 2.89 (d, J = 16.7 Hz, 1 H), 3.18 (d, J = 16.7 Hz, 1 H), 3.71 (s, 3 H), 3.74 (s, 3 H), 3.78 (s, 3 H), 3.80 (s, 3 H), 4.23 (s, 1 H), 12.06 (s, 1 H) ppm. ^{13}C ($CDCl_3$): δ = 36.8 (CH_2), 39.3 (CH_3), 52.2 (CH_3), 52.6 (CH_3), 53.2 (CH_3), 53.4 (CH_3), 62.1 (CH), 71.2 (C), 96.3 (C), 169.4 (C), 169.5 (C), 169.9 (C), 170.4 (C), 172.2 (C) ppm. $C_{14}H_{19}NO_9$ (345.31): calcd. C 48.70, H 5.55, N 4.06; found C 48.77, H 5.56, N 4.63.

CCDC-778712 (for **4c**), -778713 (for **4e**) and -778714 (for **6a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C spectra of all new compounds, X-ray crystal structures for **4c**, **4e** and **6a**.

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