The Photo-Dehydro-Diels–Alder (PDDA) Reaction – A Powerful Method for the Preparation of Biaryls

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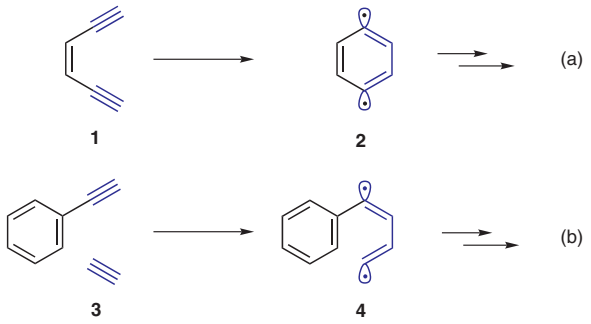
Abstract: The photochemically initiated dehydro-Diels–Alder (PDDA) reaction is an efficient and versatile method for the preparation of biaryls. The ring closure may take place both inter- and intramolecularly, of which the intramolecular variant is more productive from the preparative point of view. A variety of linkers can be employed to connect the ynone moiety, which acts as the chromophore, with another acetylene group, thus allowing large structural versatility. Principles influencing the site selectivity of the PDDA reaction will also be discussed here.

Key words: photochemistry, biaryls, alkynes, photo-dehydro-Diels–Alder reaction, cyclizations



Scheme 1 Comparison of Bergman cyclization (a) with the dehydro-Diels–Alder reaction (b)

Introduction

Acetylenes are intriguing synthetic building blocks for a vast number of synthetic applications.[1] Most of these are based on substitution reactions at one of the acetylenic atoms,[1a,2] oxidative coupling of two acetylenes,[3] addition reactions,[1a,4] as well as alkyne metathesis.[5] Compared with these well-established methods, little has been published about preparative applications relying on the addition of two acetylenic moieties to form one C–C bond in the initial step.[6] Two reactions pursuing this approach, and that have at first glance little to do with one another, are the Bergman cyclization[7] and the dehydro-Diels–Alder (DDA) reactions (Scheme 1, reactions a and b, respectively). Both reactions have in common the formation of highly reactive buta-1,3-diene-1,4-diyl diradicals **2** and **4** as primary intermediates.

The critical difference between these reactions is the formation of an aromatic system in the Bergman cyclization (Scheme 1, reaction a), which adds a considerable thermodynamic driving force to this process. The dehydro-Diels–Alder reaction, on the other hand, is highly endothermic in the first step (Scheme 1, reaction b).

In the last years, the Bergman cyclization has attracted considerable attention, because the enediyne moiety (e.g., in **1**) is often found in natural products and is responsible for a unique mode of DNA attack.[8] Calicheamycin, one of the most prominent examples, has an extremely high potency against tumor cells, and the research activities in this area culminated in the fascinating total synthesis by Nicolaou in 1992.[9] Admittedly, there are only few examples for the preparative utilization of the Bergman cyclization.[10]

The thermally initiated DDA reaction has been known for a long time, but almost seems to have fallen into oblivion. Already in 1895 Michael and Bucher reported the dimerization of phenylpropiolic acid upon prolonged heating in acetic anhydride.[11] Twelve years later Pfeiffer and Möller described a similar reaction of ethyl phenylpropiolate under drastic conditions (200 °C, sealed tube).[12] Subsequently, some preparative applications have been published, proving the scope of the reaction.[13] In contrast to these classic examples of the DDA reaction, considerable improvement was achieved by transition-metal catalysis. Thus, palladium,[14] rhodium,[15] and nickel[16] catalysts have been used in the DDA reaction.

In connection with our long-standing investigations of the Norrish–Yang reaction,[17] we were interested in structural modifications of benzoyl chromophores, which up to then had mostly been used for alleviating oxidative degradation after photochemical cyclization. To this end, we irradiated 1-phenylhex-1-yn-3-one (**5a**) but obtained, to our surprise, not the expected Yang product **6** but the naphthalene **7a** as product of a photo-dehydro-Diels–Alder (PDDA) reaction (Scheme 2).[18] We subsequently thoroughly investigated this interesting cyclization reaction and developed it into a versatile method for the preparation of biaryls. In this feature article we wish to report comprehensively on previous and new results towards the PDDA reaction. (For better clarity, the dienophile moiety will be colored blue in the graphical representations from here onwards.)

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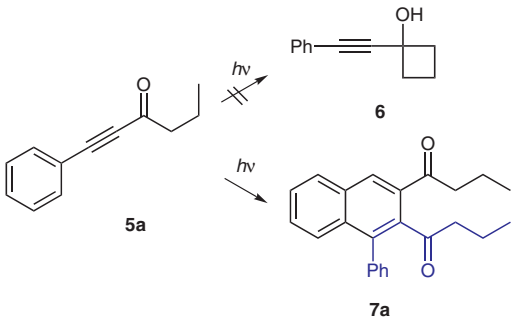


Scheme 2 Yang cyclization versus photo-dehydro-Diels–Alder reaction of an ynone

Mechanistic Model

The mechanism of the PDDA reaction was discussed in detail in our previous publications,[18a,19] and here only the most important points will be summarized. It should be noted that our present knowledge about the mechanism is solely based on DFT calculations; short-time spectroscopic investigations are currently underway. The reaction commences with a photochemical n–π* excitation of 3-arylalkynones **8** followed by an efficient intersystem crossing (ISC) to the triplet state (Scheme 3). The triplet energy of the 3-arylalkynone moiety amounts to about 250 kJ/mol. The approach of one acetylene to the other proceeds via the transition state **10a** (Scheme 3), the energy of which lies only 13–25 kJ/mol above that of the excited reactants. (Note that substituents R^1 and R^2 may be connected; see the section 'Intramolecular PDDA Reac-

Biographical Sketches

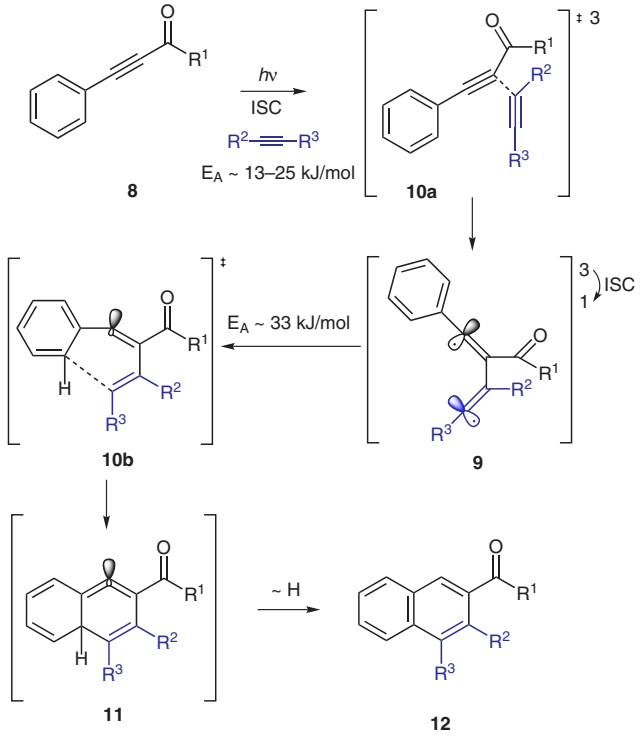
Pablo Wessig (above right), born in Görlitz in 1962, completed his PhD degree at the Humboldt University of Berlin under the supervision of Prof. Dr. H.-G. Henning in 1990. After a postdoctoral research fellowship (FCI) at the University of Basel, Switzerland, in the group of B. Giese in 1993, he obtained his habilitation degree in the group of G. Szeimies at the Humboldt University in 2000. Since 2003 he has been working as a Heisenberg fellow of the DFG at the same university. His primary research interests are focused on preparative organic photochemistry, molecular probes, and rigid molecular sticks.

Gunnar Müller (above left), born in Salzwedel in 1976, studied chemistry at the Humboldt University of Berlin. In 2002 he joined the group of Dr. P. Wessig and is currently working on his PhD thesis. His research interests include the photochemical preparation of indanones by spin-center shift and the preparative application of the PDDA reaction.

Charlotte Pick (below left), born in Bad Soden a. Ts. in 1977, studied chemistry at the Philipps University in Marburg. After she had obtained her diploma in the group of Prof. Dr. U. Koert she joined the group of Dr. P. Wessig in 2005. For her PhD degree she is working in the field of the PDDA reaction and its synthetic applications.

Annika Matthes (below right), born 1980 in Berlin, started her studies in chemistry at the Humboldt University in 2000. In 2006 she joined the group of Dr. P. Wessig to work towards her diploma degree.

tion' below.) As a result, buta-1,3-dien-1,4-diyl diradicals **9** form in a strongly exothermic process (ΔE ~ –147 kJ/mol). Diradicals **9** seem to play a key role in the mechanism. The DFT calculations with different systems revealed that the triplet and singlet states of **9** have nearly the same energy, and that activation energies of all possible consecutive steps are too high at the triplet potential energy surface (>84 kJ/mol). Consequently, we assume that at the stage of **9** the electronic state returns to the singlet potential-energy surface. With a relatively low barrier of 33 kJ/mol, one of the diradical centers now attacks an *ortho* position of the opposite aromatic ring and gives, via transition state **10b**, the cyclic allene **11** (Scheme 3). The last step to the naphthalenes **12** is a formal 1,3-hydrogen shift, but we found experimentally that this process is always mediated by the solvent.



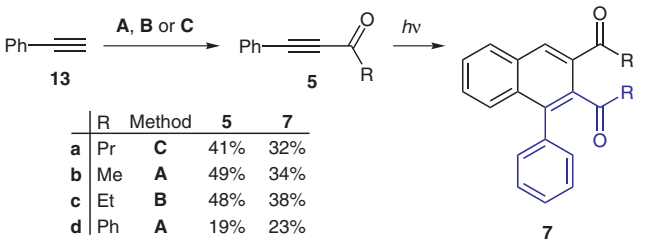
Scheme 3 Mechanism of the PDDA reaction

Besides this main reaction path we occasionally observed a cyclization of diradicals **9** to cyclobutadienes, which reacted with the protic solvent, and a cleavage reaction comparable with the Norrish type II cleavage.[19]

Synthetic Applications

Intermolecular PDDA Reaction

As mentioned above, we discovered the PDDA reaction with the dimerization of 1-phenylhex-1-yn-3-one (**5a**).[20] This reaction could also be observed with some other ynones **5b–d** (Scheme 4),[20] which were prepared from phenylacetylene (**13**) by different methods. Unfortunately, we obtained naphthalenes **7** only in relatively low yields (Scheme 4).[18a]



	R	Method	5	7
a	Pr	C	41%	32%
b	Me	A	49%	34%
c	Et	B	48%	38%
d	Ph	A	19%	23%

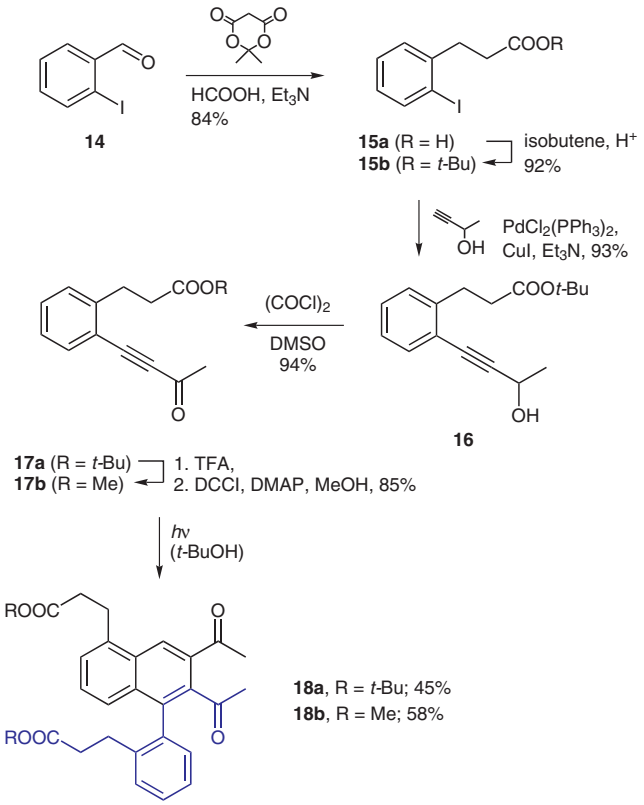
Scheme 4 Intermolecular PDDA reaction of **5a–d**. *Reagents and conditions*: Method A: 1. BuLi, 2. RCO_2Et, $BF_3{\cdot}OEt_2$; Method B: 1. BuLi, 2. $CdCl_2$, 3. RCOCl; Method C: 1. BuLi, 2. RCHO, 3. DMP.[21]

In the preceding discussion it has not yet been mentioned that the biaryls obtained by the PDDA reaction are potentially axially chiral compounds. It is expected that the introduction of at least one substituent in the *ortho* position of the dienophile aryl group should increase the rotational barrier of the biaryl axis to such an extent that the atropisomers could be resolved at room temperature.[22]

Enantiomerically pure axially chiral biaryls play a very important role as chiral ligands in asymmetric transition-metal catalysis[23] and as chiral auxiliaries[24] for many applications. Even though the asymmetric synthesis of axially chiral atropisomers by the PDDA reaction is not a subject of this article, we will present results that point in this direction. In this connection, the synthesis of axially chiral dicarboxylic acid derivatives **18** (Scheme 5) is worth mentioning. It commences with *o*-iodobenzaldehyde (**14**), which was converted in one step and in excellent yields into the 3-arylpropionic acid **15a**[25] by treatment with Meldrum's acid[26] in a mixture of formic acid and triethylamine.[27] After protection of the carboxyl group as a *tert*-butyl ester (**15b**), a Sonogashira coupling[28] with but-1-yn-3-ol afforded the propargyl alcohol **16**, which was converted into ketone **17a** by Swern oxidation. To investigate the influence of the ester group, we performed an exchange of the protective group in two steps to give the methyl ester **17b**. Upon irradiation in *tert*-butyl alcohol, esters **17** dimerized into diesters **18** in moderate to good yields.

Remarkably, the enantiomers of compounds **18** could be resolved by chiral HPLC, albeit only after extensive optimization of the conditions. The corresponding chromatograms as well as the resolution factors are depicted in Figure 1.

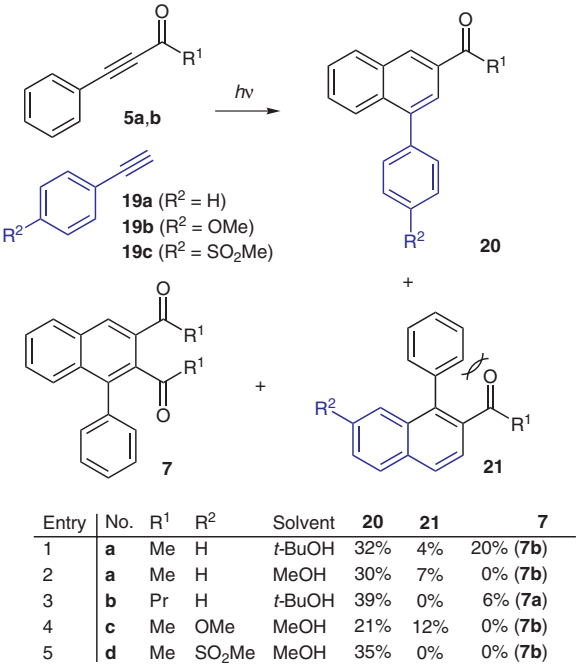
The hitherto discussed PDDA reactions have in common that ring closure took place between two identical molecules. Bearing in mind that the excited ynones are highly electrophilic species, we hypothesized that a selective cross-PDDA reaction should be possible between an ynone (which is photochemically excited) and a more electron-rich arylacetylene. Thus, we irradiated compounds **5a**,**b** in the presence of equimolar amounts of phenylacetylene (**19a**) as well as the electron-rich (4-



Scheme 5 Synthesis of diesters **18** by the PDDA reaction

methoxyphenyl)acetylene (**19b**) and the electron-poor (4-methylsulfonylphenyl)acetylene (**19c**) to investigate the influence of the substituents (Scheme 6).

It should be noted that an excess of arylacetylenes **19**[29] shortened the irradiation times, but did not influence the product yields, and complicated their purification. In all cases we observed a conspicuous preference for the cross-coupling products **20** and **21** (Scheme 6). Furthermore, the arylacetylenes **19** acted preferentially as the dienophile component, giving compounds **20** as the main products. We assume that steric hindrance in the intermediate diradicals is responsible for these results, because compounds **21** are *ortho*-disubstituted. When we used *tert*-butyl alcohol as solvent, the dimerization products **7** were obtained as minor products (Table in Scheme 6, entries 1, 3).



Entry	No.	R^1	R^2	Solvent	20	21	7
1	**a**	Me	H	*t*-BuOH	32%	4%	20% (**7b**)
2	**a**	Me	H	MeOH	30%	7%	0% (**7b**)
3	**b**	Pr	H	*t*-BuOH	39%	0%	6% (**7a**)
4	**c**	Me	OMe	MeOH	21%	12%	0% (**7b**)
5	**d**	Me	SO_2Me	MeOH	35%	0%	0% (**7b**)

Scheme 6 Intermolecular cross-PDDA reaction

Compared with phenylacetylene (**19a**), acetylene **19b** containing a donor substituent leads to lower regioselectivity (**20**/**21**) (Table in Scheme 6, entry 2 vs entry 4), whereas the strong electron-withdrawing group in **19c** resulted in the formation of only **20** (entry 5).

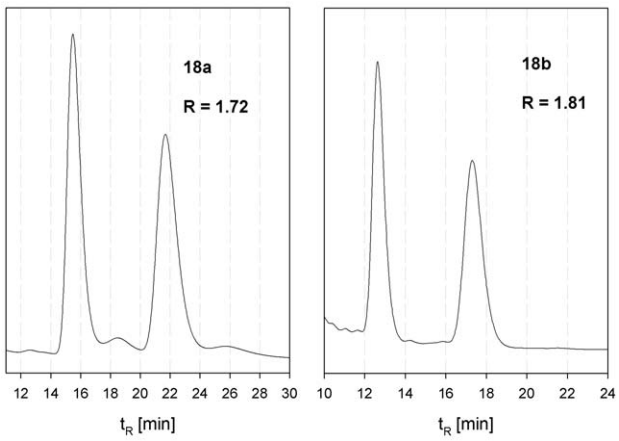


Figure 1 HPLC resolution [Chiralcel OD (Daicel), hexane–EtOH, 90:10 (**18a**), 80:20 (**18b**), flow rate 0.5 mL/min; R = resolution factor] of enantiomers of diesters **18**

Intramolecular PDDA Reaction

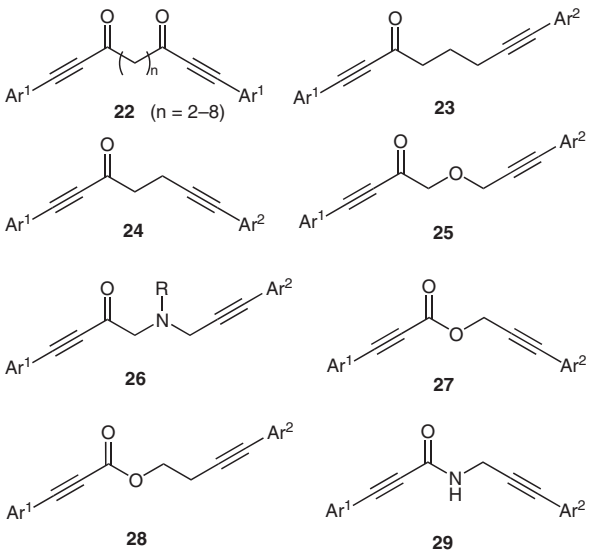
It is well known from a great variety of organic reactions that the presence of both reaction centers in the same molecule, i.e. an intramolecular reaction, is strongly favored over the intermolecular variant.

This also applies to photochemical reactions, but here it is not only a consequence of entropic influence. The limited lifetime of an electronically excited molecule may even completely prevent an intermolecular reaction if the concentration of the reactants is too low. With the intermolecular PDDA reaction we found that the reaction rates are almost always relatively low and this can, at least partly, be attributed to these reasons. Therefore we also investigated the intramolecular PDDA reaction, and for this purpose we developed a range of linkers.

In Scheme 7, eight reactant systems **22**–**29** with different linker units are summarized. The symmetric diketones **22**[30] were prepared to investigate the influence of the linker length on the yields of the PDDA reactions. Four of the

remaining nonsymmetric systems are ketones (**23**–**26**), two are esters (**27**, **28**), and the last one is an amide (**29**). The linker chains of nonsymmetric systems **23**–**29** consist of three (**24**, **27**, **29**) or four (**23**, **25**, **26**, **28**) atoms resulting in the formation of five- or six-membered rings in the PDDA reaction.

We will below briefly discuss the synthetic route to each system, without going into all details, as well as the photochemical behavior.



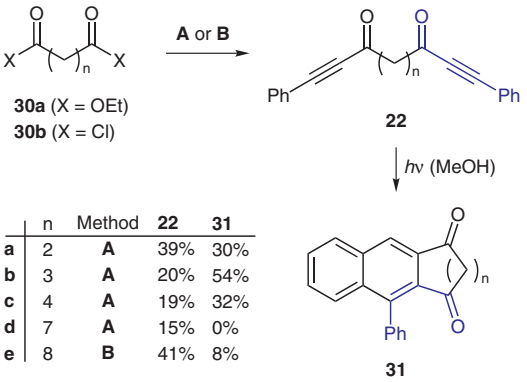
Scheme 7 Systems for the intramolecular PDDA reaction

Symmetric Diketones **22**

The symmetric diketones **22a**–**e** (Scheme 8) are accessible either by reaction of the corresponding diesters **30a** with lithium phenylacetylide in the presence of boron trifluoride diethyl etherate (method A) or from the diacid dichlorides **30b** upon treatment with cadmium phenylacetylide (method B). Unfortunately, the yields were low with both methods. The irradiation of diketones **22** in methanol afforded the desired naphthalenes **31** in moderate to good yields if two, three, or four methylene groups link the two ynone moieties (Scheme 8). Not surprisingly, the formation of **31d** bearing seven methylene groups failed, because the formed cyclic diketone ring would have an unfavorable ring size of 11 atoms. A further extension of the linker group (n = 8) gave the macrocyclic compound **31e**, albeit in low yield (Scheme 8).

Diynones **23** and **24**

Compounds **23** and **24** were prepared by a similar methodology (Scheme 9). The alcohols **32** play a key role and were obtained either from arylacetylenes by treatment with oxetane after lithiation (method A) or by Sonogashira coupling of iodoarenes with appropriate (hydroxyalkyl)acetylenes (method B). The aldehydes **33**,[31] obtained from alcohols **32**[32] by oxidation, reacted with lithium arylacetylides to form secondary propargyl alcohols and afforded, after renewed oxidation, the target ketones **23** and **24** (Scheme 9).



	n	Method	22	31
a	2	A	39%	30%
b	3	A	20%	54%
c	4	A	19%	32%
d	7	A	15%	0%
e	8	B	41%	8%

Scheme 8 Synthesis and PDDA reaction of diketones **22**. *Reagents and conditions*: Method A: 1. BuLi, 2. RCO_2Et, $BF_3{\cdot}OEt_2$; Method B: 1. BuLi, 2. $CdCl_2$, 3. RCOCl.

In contrast to the case of symmetric diketones **22**, two isomeric PDDA reaction products can form upon irradiation of ketones **23**[33] and **24**.[33] The results of the irradiation experiments are summarized in Scheme 9 and Table 1. Site selectivity was low with the parent diphenyl compounds (Table 1, entries 1, 3) and neither electron-donating groups (entries 4, 5) nor electron-withdrawing groups tethered to Ar^2 (entries 7, 9) had a significant influence on the selectivity. On the other hand, if the electron-withdrawing group is present in the aromatic ring connected to the ynone moiety, the site selectivity is considerably enhanced and reaches a ratio of up to 7:1 (entries 6, 8). Particularly striking is the photochemical behavior of reactants bearing a 1-naphthyl group as one of the two aryl residues. If the naphthyl moiety is attacked at the stage of the diradicals **9** (see Scheme 3), phenanthrenes **36** or **39** form, otherwise the 1,1′-binaphthyls **37** or **38** result. The observed site selectivity was also low if the naphthyl groups were not substituted in 2-position (entries 2, 10), but could be enhanced by introduction of a blocking group (Me or OMe), albeit with low overall yields (entries 12, 13).

We also investigated the reaction of **24** bearing a mesityl group to find out if methyl groups in the *ortho* position are able to prevent attack of the phenyl ring, and found that alkyl groups are only partly suitable because of their tendency to migrate to the adjacent position.[18a]

Diynones **25** and **26**

In view of the synthesis of biaryls fused with a heterocyclic ring, we developed ethers **25**[19] and the protected amine **26** (Scheme 10). The synthesis of **25a**–**g** commences with ethyl glycolate **40**,[19] which was alkylated with propargyl bromide followed by Sonogashira coupling with an aryl iodide Ar^2I (Scheme 10). The target compounds **25** were accessible via the Weinreb amides **43**.[19] The nitrogen analogue **26** was prepared similarly, with the

Table 1 Photochemical Behavior of Compounds **23** and **24**

Entry	Starting material	Method[a]	Ar^1	Ar^2	n	Products[b]	Yield (%)	Product ratio
1	**23a**	B	Ph	Ph	2	**34a**, **35a**	87	1:1.4
2	**23b**	B	Ph	1-naphthyl	2	**36a**, **37a**[34]	30	1:1.4
3	**24a**	A	Ph	Ph	1	**34b**, **35b**[18a]	74	1:2
4	**24b**	A	Ph	PMP	1	**34c**, **35c**[18a]	87	1:1.9
5	**24c**	A	PMP	Ph	1	**34d**, **35d**[18a]	87	1:1.7
6	**24d**	A	4-ClC_6H_4	Ph	1	**34e**, **35e**[18a]	73	1:4.6
7	**24e**	A	Ph	4-ClC_6H_4	1	**34f**, **35f**[18a]	54	1.5:1
8	**24f**	A	4-$F_3CC_6H_4$	Ph	1	**34g**, **35g**[18a]	69	1:7.3
9	**24g**	A	Ph	4-$F_3CC_6H_4$	1	**34h**, **35h**[18a]	68	1.7:1
10	**24h**	B	Ph	1-naphthyl	1	**36b**, **37b**[18a]	52	1:1.3
11	**24i**	B	1-naphthyl	Ph	1	**38a** (R = H), **39a**[18a]	67	2:1
12	**24j**	B	2-methyl-1-naphthyl	Ph	1	**38b** (R = Me)	40	–
13	**24k**	B	2-methoxy-1-naphthyl	Ph	1	**38c** (R = OMe)[34]	18	–

[a] Preparation of **23** and **24**: Reagents and conditions: Method A: 1. BuLi, 2. oxetane; Method B: Sonogashira coupling.
[b] Analytical data of the new compounds are collected in Table 5.

difference that the 3-phenylpropargyl moiety was introduced in one step.

To explore the influence of substituents in the linker on the site selectivity, we also prepared compounds **25h–k** following a slightly different approach (Scheme 10). Thus, aldehydes **47**[19] were converted into propargyl alcohols **48**[19] by treatment with lithium phenylacetylide followed by alkylation with bromoacetic acid (**49**). The remaining steps are the same as for **25a–g** (Scheme 10).

We initially expected the photochemical behavior of **25** to be very similar to that of **23** and **24**. To our surprise, the seemingly slight structure modification caused appreciable changes in the PDDA reaction (Scheme 11, Table 2). In contrast to compounds **24**, the introduction of the same electron-withdrawing groups (Cl, CF_3) has only a marginal influence on the site selectivity of the PDDA reaction (Table 2, entries 2–4). To our delight, the even stronger electron-withdrawing mesyl group, as indicated by the higher Hammett-constant,[35] considerably enhanced the selectivity in favor of **52** (Table 2, entry 5). The photochemical behavior of **25f**,**g** bearing a 1-naphthyl group was also unexpected. Instead of the PDDA reaction, only the cleavage products formed.[19]

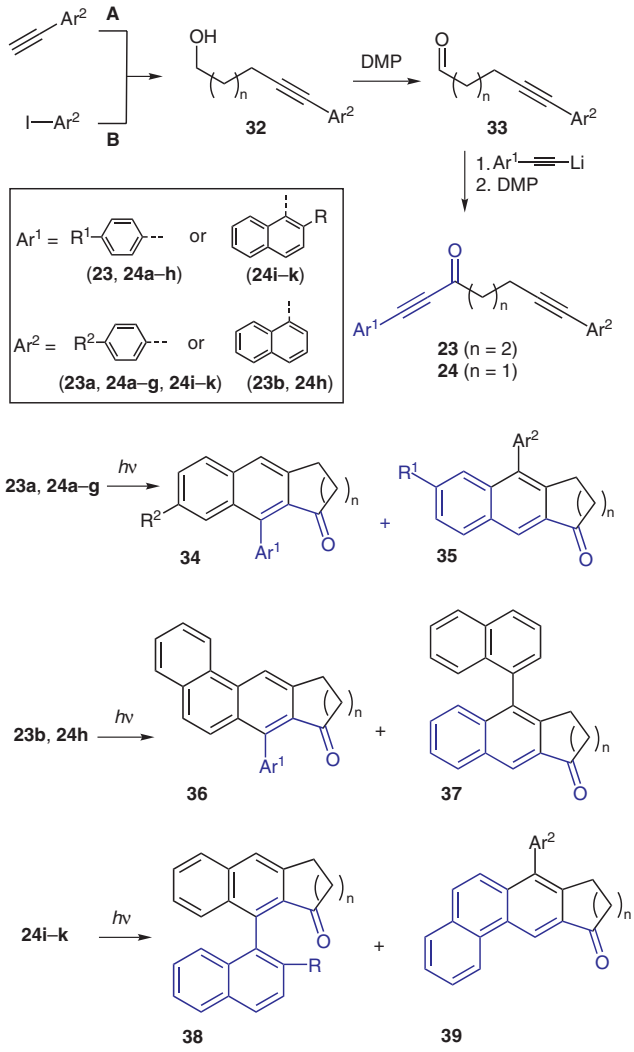
A second approach to influencing the site selectivity is based on steric repulsion, and was investigated with compounds **25h–k** (Scheme 11). Even the introduction of a methyl group inverts the site selectivity in favor of **54** (cf. Table 2, entry 1 and Table 3, entry 1), albeit marginally. The considerably larger phenyl group has nearly the same effect, presumably owing to a π-stacking effect between the two facing phenyl groups in **55**, which partly compensates the steric repulsion (Table 3, entry 2). An isopropyl group enhances the selectivity to 1:2.3 (Table 3, entry 3) and with a *tert*-butyl group only product **54k** formed (Table 3, entry 4).

The irradiation of *N*-tosylamide **26** in methanol gave products **56** and **57** in 39% yield and in an isomeric ratio of 1.6:1 (Scheme 11).

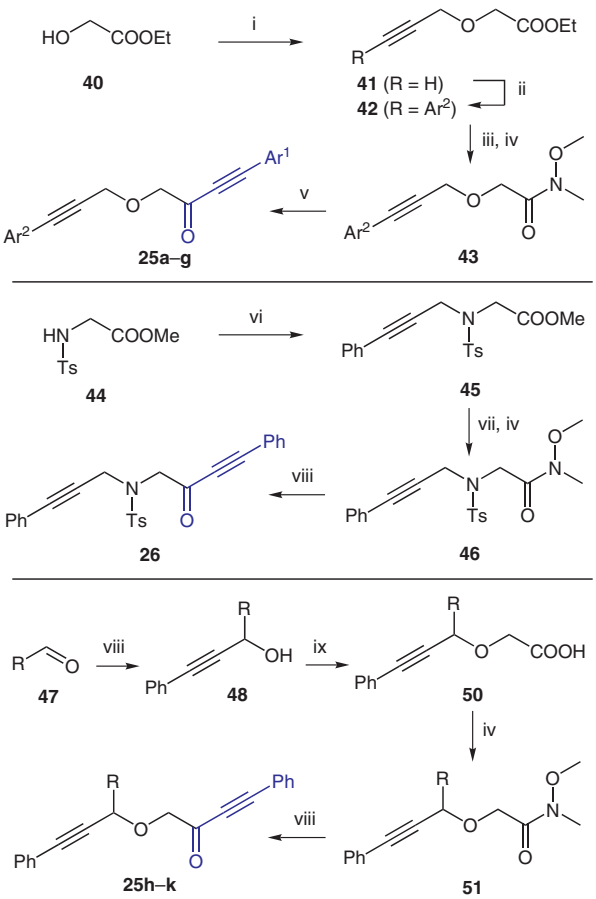
Esters **27** and **28**

In the preceding sections, the chromophoric group was always an ynone, and we assumed for the moment that this would be a structural prerequisite for the PDDA reaction. On the other hand, these ketones required relatively laborious syntheses, as discussed above. Furthermore, linkers bearing a keto group cannot be cleaved easily after ring closure, and this is a disadvantage with regard to further synthetic modifications of the biaryls prepared by the PDDA reaction. For these reasons we decided to investigate whether ester groups can be used instead of ketones as linkers.

Esters **27** and **28** are easily accessible (Scheme 12, Table 4) from propargyl alcohols **58**[34] and homopropargyl alcohols **59**,[34] respectively, either by direct esterification with the appropriate 3-arylpropiolic acids in the presence of DCC/DMAP (method A) or by conversion with phosgene into the chloroformates and treatment with lithium arylacetylides (method B).



Scheme 9 Synthesis and PDDA reaction of compounds **23** and **24**



Scheme 10 Synthesis of compounds **25** and **26**. *Reagents and conditions:* (i) Propargylbromide, NaH; (ii) Ar^2I, $PdCl_2(PPh_3)_2$, CuI (cat.), $(i\text{-}Pr)_2NH$; (iii) NaOH; (iv) H(Me)NOMe·HCl, TBTU, $(i\text{-}Pr)_2NEt$; (v) $Ar^1C{\equiv}CLi$; (vi) $PhC{\equiv}CCH_2OMs$, NaH; (vii) KOH; (viii) $PhC{\equiv}CLi$; (ix) $BrCH_2CO_2H$ (**49**), NaH.

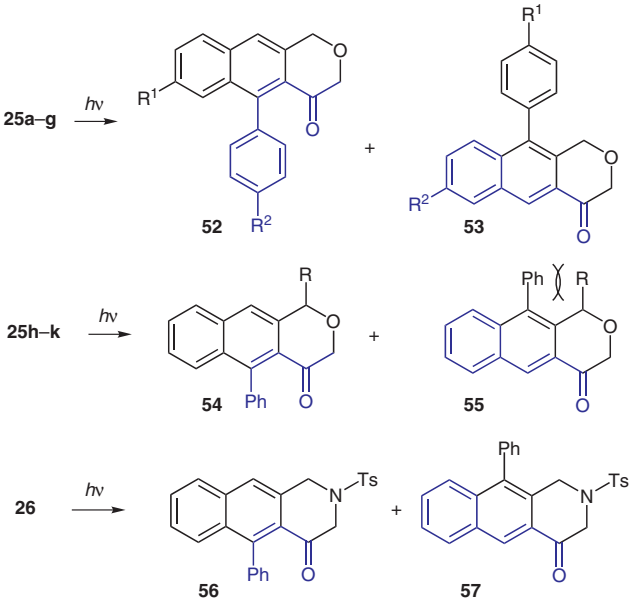
The substituents Ar^1 and Ar^2 in esters **27** and **28** were chosen according to two main criteria. On the one hand, the goal was to elucidate the influence of blocking groups in the *ortho* positions of aryl groups on site selectivity. On the other hand, we wanted to prepare the interesting substance class of 1,1′-binaphthyls.[34]

Our first irradiation experiments with esters **27** and **28** under the previously employed conditions were disappointing. The compounds showed very low photochemical reactivity in various solvents and unselective decomposition upon prolonged irradiation times. The supposition that the esters absorb UV light at wavelengths too short

Table 2 PDDA Reaction of Ketones **25a–g**[19]

Entry	Starting material	Ar^1	Ar^2	Solvent	Yield[a] (%)	Ratio **52/53**
1	**25a**	Ph	Ph	*t*-BuOH	77	1.3:1
2	**25b**	4-ClC_6H_4	Ph	MeCN	42	1.7:1
3	**25c**	Ph	4-ClC_6H_4	MeOH	52	1.2:1
4	**25d**	4-$F_3CC_6H_4$	Ph	*t*-BuOH	34	2.4:1
5	**25e**	4-MsC_6H_4	Ph	*t*-BuOH	46	6.6:1
6	**25f**	1-naphthyl	Ph	MeCN	–	–
7	**25g**	Ph	1-naphthyl	MeCN	–	–

[a] Yield of products **52** and **53** combined.



Scheme 11 PDDA reactions of ketones **25** and **26**

for our equipment (see experimental part) could soon be ruled out.

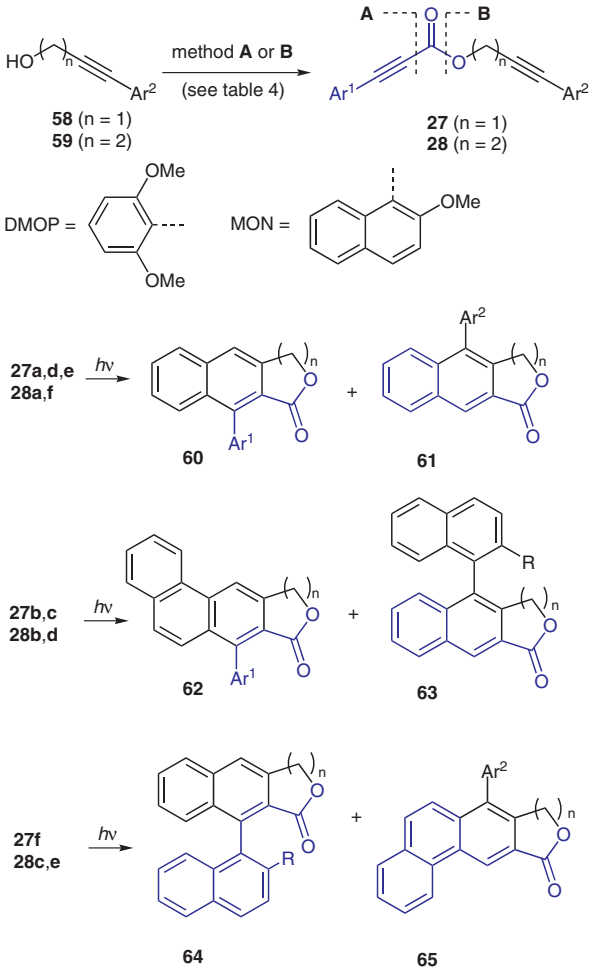
Therefore we hypothesized that the efficiency of intersystem crossing to the triplet state, necessary for the PDDA reaction, is too low, compared with the above-discussed ketones. To prove this, we irradiated esters **27** and **28** in acetone as triplet sensitizer[37] and observed, to our delight, a dramatically increased reactivity.

The results are summarized in Scheme 12 and Table 4. Not surprisingly, in the absence of blocking groups both isomeric PDDA reaction products always formed in nearly the same amounts (Table 4, entries 1, 2, 7–9). Replacement of both *o*-hydrogen atoms of phenyl (entry 4, 12) or of the hydrogen atom in the 2-position of naphthyl (entries 3, 6, 10, 11) by a methoxy group suppressed the formation of one isomer. The photochemical behavior of **27e** (entry 5) verified that methyl groups are also suited to protect a phenyl ring from attack in the PDDA reaction. Although it is obviously possible to prevent the formation of mixtures of isomers in the course of the PDDA reaction by blocking groups, the yields never exceed 50%. We presume that undesirable attack at blocked positions takes

Table 3 PDDA Reaction of Ketones **25h–k**

Entry	Starting material	R	Yield[a] (%)	Ratio **54/55**
1	**25h**	Me	68	1:1.5
2	**25i**	Ph	55	1:1.6
3	**25j**	*i*-Pr	62	1:2.3
4	**25k**	*t*-Bu	41	–

[a] Yield of products **54** and **55** combined.



Scheme 12 Synthesis and PDDA reactions of esters **27** and **28**

place nevertheless, but that this results in the molecules undergoing undefined decomposition.

Amides **29**

The usability of the last linker system, the secondary amides **29**, was demonstrated with the parent compound **29a**, the synthesis and PDDA reaction of which is depicted in Scheme 13. The very short and simple route to **29a** consists of the coupling of 3-phenylpropiolic acid (**66**)[38] with propargylamine (**67**),[38] followed by Sonogashira coupling of the resulting amide **68**[39] with iodobenzene. Upon irradiation, amide **29a**[40] cyclized to a mixture of the two isomeric PDDA reaction products **69a**[40] and **70a**,[40] in 49% yield and in an isomeric ratio of 1:1.8 (Scheme 13).

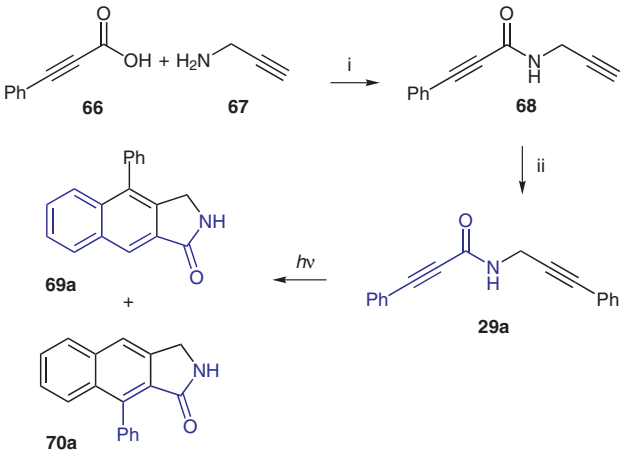
Summary and Outlook

We have demonstrated that the PDDA reaction is a powerful method for the preparation of various biaryls. The reaction can be performed intermolecularly as dimerization of ynones or addition of ynones to acetylenes, but this gives products in relatively low yields. Considerable im-

Table 4 Synthesis and PDDA Reactions of Esters **27** and **28**[a]

Entry	Starting material	Ar^1	Ar^2	n	Method[b]	Yield[c] (%) of **27** or **28**	PDDA products[d]	Yield[e] (%)	Ratio[e]
1	**27a**[36]	Ph	Ph	1	A	90	**60a** + **61a**	68	1:1.1
2	**27b**[34]	Ph	1-naphthyl	1	A	96	**62a** + **63a**	79	1:1.1
3	**27c**[34]	Ph	2-methoxy-1-naphthyl	1	A	40	**63b**	46	–
4	**27d**	2,6-$(MeO)_2C_6H_3$	Ph	1	A	100	**60b**	34	–
5	**27e**	Mes	Ph	1	A	100	**60c**	38	–
6	**27f**[34]	2-methoxy-1-naphthyl	Ph	1	A	100	**64a** (R = OMe)	36	–
7	**28a**	Ph	Ph	2	A	88	**60d** + **61b**	81	1:1.4
8	**28b**[34]	Ph	1-naphthyl	2	A	98	**62b** + **63b**	71	1.4:1
9	**28c**[34]	1-naphthyl	Ph	2	B	46	**64b** + **65a**	59	1:1.6
10	**28d**[34]	Ph	2-methoxy-1-naphthyl	2	A	91	**63c** (R = OMe)	38	–
11	**28e**[34]	2-methoxy-1-naphthyl	Ph	2	B	54	**64c** (R = OMe)	28	–
12	**28f**	2,6-$(MeO)_2C_6H_3$	Ph	2	A	91	**60e**	28	–

[a] Analytical data of new compounds are given in Table 5.
[b] Preparation of **27** and **28** from **58** or **59**. Reagents and conditions: Method A: **58** or **59**, $Ar^1C{\equiv}CCO_2H$, DCC/DMAP; Method B: 1. **58** or **59**, $COCl_2$, 2. $Ar^1C{\equiv}CLi$.
[c] Yield of product **27** or **28** from **58** or **59**.
[d] PDDA reaction products; see Scheme 12. Irradiation was performed in acetone.
[e] Yields and ratios of PDDA reaction products.



Scheme 13 Synthesis and PDDA reaction of amide **29a**. *Reagents and conditions*: (i) DCC (1.1 equiv), DMAP (6 mol%); (ii) PhI, $Pd(PPh_3)_2Cl_2$ (3 mol%), CuI (10 mol%), *i*-Pr_2NH (1 equiv).

provement can be achieved by connecting these two moieties by a linker. For this purpose, we have developed eight linker systems, each associated with special characteristics regarding synthesis and photochemistry. A disadvantage at first glance is that almost always two isomers are possible by the PDDA reaction (with the exception of dimerization and cyclization of symmetric reactants). We have, fortunately, learnt to influence this outcome by the introduction of blocking or shielding groups in the reactants.

One of the most fascinating properties of biaryls is their potential atropisomerism. Therefore, our future efforts will be focused on the stereoselective synthesis of enantiomerically pure biaryls on the basis of the results presented in this article.

The irradiations of the appropriate acetylenes or diacetylenes were performed in MeOH, *t*-BuOH, or MeCN (ketones) or acetone (esters and amides) at concentrations of 0.01 mmol/mL. A high-pressure mercury arc lamp (150 W) was used. Light of wavelength <300 nm was absorbed by a Pyrex glass jacket between the lamp and the reaction vessel. The reactions were monitored by TLC to determine when the reactants had completely disappeared. The solns were concentrated under reduced pressure and the crude residues were purified by flash chromatography to give the pure photoproducts. ^1H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded on a Bruker DPX-300 spectrometer. $CDCl_3$ was used as the solvent for NMR measurements and TMS was used as internal reference. The ESI-HRMS and EI-HRMS were carried out on a MSI Concept 1H mass spectrometer. The analytical data of the new compounds described here are given in Table 5.

Table 5 Analytical Data of New Compounds

Compound	^{1}H NMR (300 MHz, $CDCl_3$): δ	^{13}C NMR (75.5 MHz, $CDCl_3$): δ	HRMS: *m/z*
15b	7.75–6.79 (m, 4 H), 2.96–2.91 (t, 2 H, ^3J = 7.8 Hz, CH_2), 2.49–2.44 (t, J = 7.8 Hz, 2 H, CH_2), 1.37 (s, 9 H, *t*-Bu)	171.8 ($C_{q/COO}$), 143.3 ($C_{q/Ar}$), 139.5 (CH_{Ar}), 129.4 (CH_{Ar}), 128.33 (CH_{Ar}), 128.0 (CH_{Ar}), 100.4 ($C_{q/Ar}$), 80.5 ($C_{q/tBu}$), 36.1 (CH_2), 35.5 (CH_2), 28.1 ($CH_{3/t\text{-}Bu}$)	(ESI) calcd for $C_{13}H_{17}O_2INa$ [M^+ + Na]: 355.0165; found: 355.0165
16	7.31–7.06 (m, 4 H, Ar), 4.73–4.66 (m, 1 H, CH), 3.24–3.18 (s, 1 H, OH), 3.00 (t, ^3J = 8 Hz, 2 H, CH_2), 2.51–2.46 (t, ^3J = 8 Hz, 2 H, CH_2), 1.50–1.48 (d, ^3J = 6.6, 3 H, CH_3), 1.35 (s, 9 H, *t*-Bu)	172.9 ($C_{q/COO}$), 142.8 ($C_{q/Ar}$), 132.0 (CH_{Ar}), 128.7 (CH_{Ar}), 128.4 (CH_{Ar}), 126.2 (CH_{Ar}), 122.2 (CH_{Ar}), 95.8 ($C_{q/acetylene}$), 82.0 ($C_{q/acetylene}$), 80.7 ($C_{q/t\text{-}Bu}$), 58.6 (CH), 36.2 (CH_2), 30.42 (CH_2), 28.1 ($CH_{3/t\text{-}Bu}$), 24.4 (CH_3)	(EI) calcd for $C_{17}H_{22}O_3$ [M^+]: 274.1569; found: 274.1569
17a	7.35–7.00 (m, 4 H, Ar), 3.46 (s, 3 H, $OCCH_3$), 2.96–2.91 (t, 2 H, CH_2, ^3J = 7.8 Hz), 2.94–2.44 (t, ^3J = 7.8 Hz, 2 H, CH_2) 2.26 (s, 3 H, CH_3)	184.4 ($C_{q/CO}$), 172.9 ($C_{q/COO}$), 144.4 ($C_{q/Ar}$), 134.0 (CH_{Ar}), 131.1 (CH_{Ar}), 129.1 (CH_{Ar}), 126.7 (CH_{Ar}), 119.3 ($C_{q/Ar}$), 92.1 ($C_{q/acetylene}$), 88.6 ($C_{q/acetylene}$) 51.7 (CH_3), 34.7 (CH_2), 32.8 (CH_3), 29.7 (CH_2)	(EI) calcd for $C_{14}H_{14}O_3$ [M^+]: 230.0943; found: 230.0943
17b	7.50–7.17 (m, 4 H, Ar), 3.08–3.02 (d, ^3J = 7.7 Hz, 2 H, CH_2), 2.56–2.51 (d, ^3J = 7.7 Hz, 2 H, CH_2), 2.15 (s, 3 H, CH_3), 1.36 (s, 9 H, *t*-Bu)	184.4 ($C_{q/CO}$), 171.8 ($C_{q/COO}$), 144.8 ($C_{q/Ar}$), 133.9 (CH_{Ar}), 131.0 (CH_{Ar}), 129.1 (CH_{Ar}), 126.5 (CH_{Ar}), 119.3 ($C_{q/Ar}$), 92.1 ($C_{q/acetylene}$), 88.9 ($C_{q/acetylene}$), 80.5 ($C_{q/t\text{-}Bu}$), 36.0 (CH_2), 32.8 (CH_3), 29.9 (CH_2), 28.0 ($CH_{3/t\text{-}Bu}$)	(EI) calcd for $C_{17}H_{20}O_3$ [M^+]: 272.1412; found: 272.1412
18a	8.70 (s, 1 H), 7.46–7.13 (m, 7 H), 2.802 (s, 3 H), 2.60–2.51 (m, 4 H), 2.36–2.29 (m, 4 H), 1.46 (s, 9 H), 1.34 (s, 9 H)	205.5 ($C_{q/CO}$), 198.8 ($C_{q/CO}$), 172.3 ($C_{q/COO}$), 140.2 ($C_{q/Ar}$), 138.6 ($C_{q/Ar}$), 135.8 ($C_{q/Ar}$) 134.9 ($C_{q/Ar}$), 131.0 (CH_{Ar}), 129.1 (CH), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 127.4 (CH_{Ar}), 127.1 (CH_{Ar}), 126.0 (CH_{Ar}), 125.6(CH_{Ar}), 80.9 ($C_{q/t\text{-}Bu}$), 80.2 ($C_{q/t\text{-}Bu}$), 36.5 (CH_2), 35.2 (CH_2), 31.6 (CH_3) 28.1 ((CH_3)$_3$), 28.0 ((CH_3)$_3$), 27.0 (CH_3)	(ESI) calcd for $C_{34}H_{41}O_6$ [M^+ + H]: 545.2903; found: 545.2898
18b	8.62 (s, 1 H), 7.03–7.38 (m, 7 H), 3.65 (s, 3 H), 3.46 (s, 3 H), 2.75–2.80 (t, ^2J = 7.8 Hz, 2 H), 2.72 (s, 3 H), 2.31–2.65 (m, 6 H), 2.07 (s, 3 H)	198.7 ($C_{q/CO}$), 173.4 ($C_{q/COO}$), 173.2 ($C_{q/COO}$), 139.9 ($C_{q/Ar}$), 130.9 (CH_{Ar}), 130.24 ($C_{q/Ar}$), 129.2 (CH_{Ar}), 125.7 (CH_{Ar}), 51.9 (CH_3), 51.45 (CH_3), 35.1 (CH_2), 33.9 (CH_2), 31.6 (CH_3), 27.9 (CH_2), 27.9 (CH_2), 27 (CH_3)	(EI) calcd for $C_{28}H_{28}O_6$ [M^+]: 460.1886; found: 460.1886
20a	8.48 (s, 1 H), 8.05–8.02 (m, 1 H), 7.99 (d, ^4J = 1.9 Hz, 1 H), 7.95–7.92 (m, 1 H), 7.58–7.50 (m, 7 H), 2.75 (s, 3 H)	198.1 ($C_{q/CO}$), 140.9 ($C_{q/Ar}$), 139.9 ($C_{q/Ar}$), 133.9 ($C_{q/Ar}$), 133.0 ($C_{q/Ar}$), 129.9 (CH_{Ar}), 129.6 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 127.6 (CH_{Ar}), 126.6 (CH_{Ar}), 126.1 (CH_{Ar}), 124.8 (CH_{Ar}), 26.7 (CH_3)	(EI) calcd for $C_{18}H_{14}O$ [M^+]: 246.1045; found: 246.1045
21a	7.91 (d, ^3J = 8.3 Hz, 2 H), 7.69 (dd, ^3J = 8.7, 8.7 Hz, 2 H), 7.58–7.37 (m, 7 H), 1.94 (s, 3 H)	204.9 ($C_{q/CO}$), 138.4 ($C_{q/Ar}$), 138.3 ($C_{q/Ar}$), 138.1 ($C_{q/Ar}$), 134.4 ($C_{q/Ar}$), 131.9 ($C_{q/Ar}$), 130.6 (CH_{Ar}), 128.5 (CH_{Ar}), 128.2 (CH_{Ar}), 128.0 (CH_{Ar}), 127.24 (CH_{Ar}), 127.22 (CH_{Ar}), 126.7 (CH_{Ar}), 124.3 (CH_{Ar}), 30.7 (CH_3)	(EI) calcd for $C_{18}H_{14}O$ [M^+]: 246.1045; found: 246.1045
20b	8.49 (s, 1 H), 8.05–8.02 (m, 1 H), 7.99 (d, ^4J = 1.5 Hz, 1 H), 7.95–7.89 (m, 1 H), 7.58–7.51 (m, 7 H), 3.11 (t, ^3J = 7.2 Hz, 2 H), 1.85 (tq, ^3J = 7.2, 7.5 Hz, 2 H), 1.06 (t, ^3J = 7.5 Hz, 3 H)	200.4 ($C_{q/CO}$), 140.8 ($C_{q/Ar}$), 140.0 ($C_{q/Ar}$), 138.81 ($C_{q/Ar}$), 138.78 ($C_{q/Ar}$), 133.0 ($C_{q/Ar}$), 129.94 (CH_{Ar}), 129.92 (CH_{Ar}), 129.0 (CH_{Ar}), 128.42 (CH_{Ar}), 128.35 (CH_{Ar}), 127.6 (CH_{Ar}), 126.6 (CH_{Ar}), 126.1 (CH_{Ar}), 124.8 (CH_{Ar}), 40.6 (CH_2), 17.9 (CH_2), 13.9 (CH_3)	(ESI) calcd for $C_{20}H_{19}O$ [M^+ + H]: 275.1436; found: 275.1434
20c	8.45 (s, 1 H), 8.04–7.94 (m, 3 H), 7.59–7.52 (m, 2 H), 7.45–7.40 (m, 2 H), 7.07–7.02 (m, 2 H), 3.90 (s, 3 H), 2.74 (s, 3 H),	198.2 ($C_{q/CO}$), 159.2 ($C_{q/Ar}$), 140.6 ($C_{q/Ar}$), 134.1 ($C_{q/Ar}$), 134.0 ($C_{q/Ar}$), 133.1 ($C_{q/Ar}$), 132.3 ($C_{q/Ar}$), 131.1 (CH_{Ar}), 130.0 (CH_{Ar}), 129.4 (CH_{Ar}), 128.5 (CH_{Ar}), 126.6 (CH_{Ar}), 126.2 (CH_{Ar}), 124.8 (CH_{Ar}), 113.9 (CH_{Ar}), 55.4 (CH_3), 26.8 (CH_3)	(EI) calcd for $C_{19}H_{16}O_2$ [M^+]: 276.1150; found: 276.1150
21c	7.83 (d, ^3J = 8.3 Hz, 1 H), 7.81 (d, ^3J = 8.9 Hz, 1 H), 7.53–7.49 (m, 4 H), 7.40–7.37 (m, 2 H), 7.21 (dd, ^3J = 8.9 Hz, ^4J = 2.5 Hz, 1 H), 6.99 (d, ^4J = 2.5 Hz, 1 H), 3.71 (s, 3 H), 1.94 (s, 3 H),	205.1 ($C_{q/CO}$), 158.2 ($C_{q/Ar}$), 138.7 ($C_{q/Ar}$), 138.5 ($C_{q/Ar}$), 136.9 ($C_{q/Ar}$), 133.9 ($C_{q/Ar}$), 133.2 ($C_{q/Ar}$), 130.4 (CH_{Ar}), 129.9 (CH_{Ar}), 129.5 (CH_{Ar}), 128.6 (CH_{Ar}), 128.1 (CH_{Ar}), 127.7 (CH_{Ar}), 122.0 (CH_{Ar}), 119.6 (CH_{Ar}), 105.6 (CH_{Ar}), 55.1 (CH_3), 30.7 (CH_3)	(EI) calcd for $C_{19}H_{16}O_2$ [M^+]: 276.1150; found: 276.1150

Table 5 Analytical Data of New Compounds (continued)

Compound	^{1}H NMR (300 MHz, $CDCl_3$): δ	^{13}C NMR (75.5 MHz, $CDCl_3$): δ	HRMS: *m/z*
20d	8.53 (s, 1 H), 8.11–8.06 (m, 3 H), 7.98 (d, ^4J = 1.7 Hz, 1 H), 7.82–7.79 (m, 1 H), 7.73–7.69 (m, 2 H), 3.16 (s, 3 H), 2.76 (s, 3 H)	197.7 ($C_{q/CO}$), 145.8 ($C_{q/Ar}$), 139.8 ($C_{q/Ar}$), 138.7 ($C_{q/Ar}$), 133.9 ($C_{q/Ar}$), 133.3 ($C_{q/Ar}$), 131.0 (CH_{Ar}), 130.7 (CH_{Ar}), 130.2 (CH_{Ar}), 129.2 (CH_{Ar}), 127.5 (CH_{Ar}), 127.1 (CH_{Ar}), 125.4 (CH_{Ar}), 124.9 (CH_{Ar}), 44.6 (CH_3), 26.6 (CH_3)	(EI) calcd for $C_{19}H_{16}O_3S$ [M^+]: 324.0820; found: 324.0818
23a	7.59–7.56 (m, 2 H), 7.48–7.35 (m, 5 H), 7.29–7.26 (m, 3 H), 2.89 (t, ^3J = 7.4 Hz, 2 H), 2.53 (t, ^3J = 6.8 Hz, 2 H), 2.04 (quin, ^3J = 7.2 Hz, 2 H)	187.3 ($C_{q/CO}$), 133.1 (CH_{Ar}), 131.6 (CH_{Ar}), 130.7 (CH_{Ar}), 128.7 (CH_{Ar}), 128.2 (CH_{Ar}), 127.7 (CH_{Ar}), 123.6 ($C_{q/Ar}$), 119.9 ($C_{q/Ar}$), 90.9 (C_q), 88.8 (C_q), 87.8 (C_q), 81.6 (C_q), 44.3 (CH_2), 23.0 (CH_2), 18.8 (CH_2)	(ESI) calcd for $C_{21}H_{16}O$ [M^+ + H]: 273.1279; found: 273.1278
24j	8.30 (d, ^3J = 8.7 Hz, 1 H), 7.86 (d, ^3J = 8.3 Hz, 1 H), 7.82 (d, ^3J = 6.8 Hz, 1 H), 7.59 (ddd, ^3J = 8.3, 6.8 Hz, ^4J = 1.5 Hz, 1 H), 7.49 (ddd, ^3J = 7.9, 6.8 Hz, ^4J = 1.3 Hz, 1 H), 7.41–7.37 (m, 3 H), 7.29–7.25 (m, 4 H), 3.17–3.11 (m, 2 H), 2.93–2.86 (m, 2 H), 2.72 (s, 3 H)	185.4 ($C_{q/CO}$), 143.0 ($C_{q/Ar}$), 131.6 (CH_{Ar}), 131.4 ($C_{q/Ar}$), 131.1 (CH_{Ar}), 128.3 (CH_{Ar}), 128.2 (CH_{Ar}), 127.9 (CH_{Ar}), 127.8 (CH_{Ar}), 126.0 (CH_{Ar}), 125.4 (CH_{Ar}), 123.4 ($C_{q/Ar}$), 94.7 (C_q), 87.8 (C_q), 44.5 (CH_2), 21.5 (CH_3), 14.5 (CH_2)	(EI) calcd for $C_{24}H_{17}O$ [M^+ – H]: 322.1279; found: 322.1280
26	7.75–7.69 (m, 2 H), 7.58–7.51 (m, 2 H), 7.50–7.38 (m, 1 H), 7.37–7.29 (m, 2 H), 7.26–7.13 (m, 5 H), 7.11–7.06 (m, 2 H), 4.42 (s, 2 H, $NCH_2C\equiv$), 4.29 (s, 2 H, NCH_2CO), 2.30 (s, 3 H, $TsCH_3$)	182.3 ($C_{q/CO}$), 143.9 ($C_{q/Ar}$), 136.1 ($C_{q/Ar}$), 133.4 (C_{Ar}), 131.6 (C_{Ar}), 131.2 (C_{Ar}), 129.7 (C_{Ar}), 128.7 (C_{Ar}), 128.6 (C_{Ar}), 128.2 (C_{Ar}), 127.6 (C_{Ar}), 121.9 ($C_{q/Ar}$), 119.4 ($C_{q/Ar}$), 94.6 (PhC≡*C*CO), 86.4 (Ph*C*≡CCO), 86.1 (Ph*C*≡CCH_2), 81.3 (PhC≡*C*CH_2), 56.4 (N*C*H_2CO), 38.6 (N*C*H_2C≡), 21.5 ($TsCH_3$)	(EI) calcd for $C_{26}H_{21}NO_3S$ [M^+]: 427.1242; found: 427.1241
27d	7.48–7.42 (m, 2 H), 7.36–7.29 (m, 4 H), 6.52 (d, ^3J = 8.5 Hz, 2 H), 5.05 (s, 2 H), 3.88 (s, 6 H)	163.2 ($C_{q/Ar}$), 153.6 ($C_{q/CO}$), 132.8 (CH_{Ar}), 132.4 (CH_{Ar}), 131.9 (CH_{Ar}), 131.6 (CH_{Ar}), 128.7 (CH_{Ar}), 128.3 (CH_{Ar}), 122.1 ($C_{q/Ar}$), 103.2 (CH_{Ar}), 98.0 ($C_{q/Ar}$), 88.0 (C_q), 86.9 (C_q), 82.4 (C_q), 81.6 (C_q), 56.1 (CH_3), 53.9 (CH_2)	(EI) calcd for $C_{20}H_{16}O_4$ [M^+]: 320.1049; found: 320.1048
27e	7.50–7.47 (m, 2 H), 7.34–7.32 (m, 3 H), 6.89 (s, 2 H), 5.06 (s, 2 H), 2.46 (s, 6 H), 2.30 (s, 3 H)	153.7 ($C_{q/CO}$), 142.7 ($C_{q/Ar}$), 140.8 ($C_{q/Ar}$), 131.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.3 (CH_{Ar}), 127.9 (CH_{Ar}), 122.0 ($C_{q/Ar}$), 116.2 ($C_{q/Ar}$), 87.4 (C_q), 87.0 (C_q), 86.1 (C_q), 82.3 (C_q), 53.9 (CH_2), 21.5 (CH_3), 20.8 (CH_3)	(EI) calcd for $C_{21}H_{18}O_2$ [M^+]: 302.1307; found: 302.1307
28a	7.62–7.59 (m, 2 H), 7.49–7.35 (m, 5 H), 7.32–7.27 (m, 3 H), 4.43 (t, ^3J = 6.8 Hz, 2 H), 2.85 (t, ^3J = 6.8 Hz, 2 H)	153.8 ($C_{q/CO}$), 133.0 (CH_{Ar}), 131.7 (CH_{Ar}), 130.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.2 (CH_{Ar}), 128.0 (CH_{Ar}), 123.2 ($C_{q/Ar}$), 119.5 ($C_{q/Ar}$), 86.8 (C_q), 84.8 (C_q), 82.3 (C_q), 80.4 (C_q), 63.7 (CH_2), 19.8 (CH_2)	(EI) calcd for $C_{19}H_{14}O_2$ [M^+]: 274.0994; found: 274.0992
28f	7.42–7.40 (m, 2 H), 7.34 (t, ^3J = 8.5 Hz, 1 H), 7.30–7.27 (m, 3 H), 6.52 (d, ^3J = 8.5 Hz, 2 H), 4.42 (t, ^3J = 7.3 Hz, 2 H), 3.88 (s, 6 H), 2.85 (t, ^3J = 7.3 Hz, 2 H)	163.1 ($C_{q/Ar}$), 154.0 ($C_{q/CO}$), 132.6 (CH_{Ar}), 131.6 (CH_{Ar}), 128.2 (CH_{Ar}), 127.9 (CH_{Ar}), 123.3 ($C_{q/Ar}$), 103.3 (CH_{Ar}), 98.0 ($C_{q/Ar}$), 88.4 (C_q), 84.9 (C_q), 82.2 (C_q), 81.0 (C_q), 63.5 (CH_2), 56.1 (CH_3), 19.8 (CH_2)	(EI) calcd for $C_{21}H_{18}O_4$ [M^+]: 334.1205; found: 334.1205
29a	7.49–7.44 (m, 2 H), 7.38–7.20 (m, 8 H), 6.22 (br s, 1 H, NH), 4.31 (d, ^3J = 5.5 Hz, 2 H, CH_2)	152.9 ($C_{q/CO}$), 132.5 (C_{Ar}), 131.7 (C_{Ar}), 130.2 (C_{Ar}), 128.6 (C_{Ar}), 128.5 (C_{Ar}), 128.3 (C_{Ar}), 122.3 ($C_{q/Ar}$), 120.0 ($C_{q/Ar}$), 85.5 (PhC≡*C*CH_2), 83.9 (Ph*C*≡CCH_2), 83.7 (Ph*C*≡CCO), 82.4 (PhC≡*C*CO), 30.4 (CH_2)	(EI) calcd for $C_{18}H_{13}NO$ [M^+]: 259.0997; found: 259.0997
34a	7.81 (d, ^3J = 8.3 Hz, 1 H), 7.75 (s, 1 H), 7.55–7.44 (m, 5 H), 7.32 (ddd, ^3J = 8.3, 8.3 Hz, ^4J = 1.4 Hz, 1 H), 7.21–7.19 (m, 2 H), 3.17 (t, ^3J = 6.2 Hz, 2 H), 2.66 (t, ^3J = 6.7 Hz, 2 H), 2.20–2.14 (m, 2 H)	199.1 ($C_{q/CO}$), 142.8 ($C_{q/Ar}$), 140.3 ($C_{q/Ar}$), 139.6 ($C_{q/Ar}$), 135.0 ($C_{q/Ar}$), 132.3 ($C_{q/Ar}$), 128.80 (CH_{Ar}), 128.78 ($C_{q/Ar}$), 128.5 (CH_{Ar}), 128.1 (CH_{Ar}), 127.9 (CH_{Ar}), 126.9 (CH_{Ar}), 126.7 (CH_{Ar}), 126.6 (CH_{Ar}), 125.7 (CH_{Ar}), 41.1 (CH_2), 31.2 (CH_2), 22.9 (CH_2)	(EI) calcd for $C_{20}H_{16}O$ [M^+]: 272.1201; found: 272.1202

Table 5 Analytical Data of New Compounds (continued)

Compound	^{1}H NMR (300 MHz, $CDCl_3$): δ	^{13}C NMR (75.5 MHz, $CDCl_3$): δ	HRMS: *m/z*
35a	8.71 (s, 1 H), 8.01–7.99 (m, 1 H), 7.55–7.37 (m, 6 H), 7.28–7.26 (m, 2 H), 2.79–2.72 (m, 4 H), 2.10–2.04 (m, 2 H)	199.1 ($C_{q/CO}$), 138.7 ($C_{q/Ar}$), 138.3 ($C_{q/Ar}$), 136.7 ($C_{q/Ar}$), 135.1 ($C_{q/Ar}$), 131.4 ($C_{q/Ar}$), 130.4 ($C_{q/Ar}$), 130.04 (CH_{Ar}), 130.00 (CH_{Ar}), 128.62 (CH_{Ar}), 128.60 (CH_{Ar}), 128.4 (CH_{Ar}), 127.4 (CH_{Ar}), 126.2 (CH_{Ar}), 125.8 (CH_{Ar}), 39.4 (CH_2), 28.5 (CH_2), 23.0 (CH_{Ar})	(EI) calcd for $C_{20}H_{16}O$ [M^+]: 272.1201; found: 272.1202
38b	8.01 (s, 1 H), 7.95 (d, ^3J = 8.3 Hz, 1 H), 7.91 (d, ^3J = 8.1 Hz, 1 H), 7.88 (d, ^3J = 7.9 Hz, 1 H), 7.56 (ddd, ^3J = 8.1, 8.1 Hz, ^4J = 1.5 Hz, 1 H), 7.50 (d, ^3J = 8.5 Hz, 1 H), 7.38–7.23 (m, 4 H), 7.13 (ddd, ^3J = 8.3, 8.3 Hz, ^4J = 1.3 Hz, 1 H), 6.83 (dd, ^3J = 7.9 Hz, ^5J = 0.6 Hz, 1 H), 3.41–3.36 (m, 2 H), 2.72–2.67 (m, 2 H), 1.99 (s, 3 H)	205.4 ($C_{q/CO}$), 148.2 ($C_{q/Ar}$), 137.5 ($C_{q/Ar}$), 136.9 ($C_{q/Ar}$), 133.9 ($C_{q/Ar}$), 132.9 ($C_{q/Ar}$), 132.3 ($C_{q/Ar}$), 132.0 ($C_{q/Ar}$), 131.9 ($C_{q/Ar}$), 128.5 (CH_{Ar}), 128.4 (CH_{Ar}), 128.00 (CH_{Ar}), 127.98 (CH_{Ar}), 127.9 (CH_{Ar}), 127.8 (CH_{Ar}), 126.3 (CH_{Ar}), 125.8 (CH_{Ar}), 125.2 (CH_{Ar}), 124.6 (CH_{Ar}), 37.2 (CH_2), 25.0 (CH_2), 20.2 (CH_3)	(EI) calcd for $C_{24}H_{18}O$ [M^+]: 322.1358; found: 322.1358
45	7.80–7.74 (m, 2 H), 7.31–7.24 (m, 5 H), 7.18–7.12 (m, 2 H), 4.48 (s, 2 H, $NCH_2C{\equiv}$), 4.16 (s, 2 H, CH_2), 3.72 (s, 3 H, CO_2CH_3), 2.37 (s, 3 H, $TsCH_3$)	168.9 ($C_{q/CO}$), 143.8 ($C_{q/Ar}$), 136.0 ($C_{q/Ar}$), 131.6 (C_{Ar}), 129.6 (C_{Ar}), 128.6 (C_{Ar}), 128.2 (C_{Ar}), 127.6 (C_{Ar}), 113.8 ($C_{q/Ar}$), 86.1 (Ph*C*≡C), 81.3 (PhC≡*C*), 52.3 (N*C*H_2CO), 47.0 (CO_2*C*H_3), 38.4 (N*C*H_2C≡), 31.5 ($TsCH_3$)	(ESI) calcd for $C_{19}H_{19}NNaO_4S$ [M^+ + Na]: 380.0927; found: 380.0922
46	7.75–7.69 (m, 2 H), 7.24–7.16 (m, 5 H), 7.12–7.06 (m, 2 H), 4.45 (s, 2 H, $NCH_2C{\equiv}$), 4.26 (s, 2 H, NCH_2CO), 3.64 (s, 3 H, OCH_3), 3.11 (s, 3 H, NCH_3), 2.29 (s, 3 H, $TsCH_3$)	168.5 ($C_{q/CO}$), 143.5 ($C_{q/Ar}$), 136.3 ($C_{q/Ar}$), 131.5 (C_{Ar}) 129.5 (C_{Ar}), 128.4 (C_{Ar}), 128.1 (C_{Ar}), 127.6 (C_{Ar}), 122.1 ($C_{q/Ar}$), 85.7 (Ph*C*≡C), 82.0 (PhC≡*C*), 61.4 (OCH_3), 46.4 (N*C*H_2CO), 38.2 (N*C*H_2C≡), 32.3 (NCH_3), 21.4 ($TsCH_3$)	(ESI) calcd for $C_{20}H_{22}N_2NaO_4S$ [M^+ + Na]: 409.1198; found: 409.1193
56/57	8.26 (s, 1 H, **57**), 7.91–7.84 (m, 1 H), 7.78 (d, ^3J = 8.1 Hz, 2 H), 7.68 (s, 1 H, **56**), 7.56 (d, ^3J = 8.1 Hz, 2 H), 7.53–7.51 (m, 2 H), 7.51–7.48 (m, 2 H), 7.46–7.44 (m, 1 H), 7.43–7.41 (m, 2 H), 7.40–7.39 (m, 3 H), 7.38–7.36 (m, 3 H), 7.33 (d, ^3J = 1.1 Hz, 1 H), 7.31 (d, ^3J = 1.1 Hz, 1 H), 7.22–7.16 (m, 2 H), 7.10 (d, ^3J = 7.9 Hz, 2 H), 7.00 (d, ^3J = 7.9 Hz, 2 H), 4.63 (s, 2 H, NCH_2C_{Ar}, **56**), 4.33 (s, 2 H, NCH_2C_{Ar}, **57**), 4.10 (s, 2 H, $COCH_2N$, **57**), 3.91 (s, 2 H, $COCH_2N$, **56**), 2.25 (s, 3 H, CH_3, **56**), 2.19 (s, 3 H, CH_3, **57**)	192.0 ($C_{q/CO}$, **57**), 191.4 ($C_{q/CO}$, **56**), 144.05 (CH_{Ar}) 144.0 ($C_{q/Ar}$), 143.7 ($C_{q/Ar}$), 138.6 (CH_{Ar}), 137.2 ($C_{q/Ar}$), 136.6 ($C_{q/Ar}$), 135.12($C_{q/Ar}$), 135.07 (CH_{Ar}), 133.8 ($C_{q/Ar}$), 133.2 (CH_{Ar}), 132.7 ($C_{q/Ar}$), 131.7 ($C_{q/Ar}$), 130.4 ($C_{q/Ar}$), 130.0 ($C_{q/Ar}$), 129.7 (CH_{Ar}), 129.62 (CH_{Ar}), 129.55 (CH_{Ar}), 129.3 ($C_{q/Ar}$), 129.1 (CH_{Ar}), 128.7 ($C_{q/Ar}$), 128.6 (CH_{Ar}), 128.3 ($C_{q/Ar}$), 128.0 (CH_{Ar}), 127.8 (CH_{Ar}), 127.5 (CH_{Ar}), 127.3 (CH_{Ar}), 127.2 (CH_{Ar}), 126.7 (CH_{Ar}), 126.3 ($C_{q/Ar}$), 125.2 (CH_{Ar}), 55.8 (CO*C*H_2N, **56**), 54.6 (CO*C*H_2N, **57**), 49.2 (N*C*H_2C_{Ar}, **56**), 47.0 (N*C*H_2C_{Ar}, **57**), 21.4 (CH_3, **56**), 15.2 (CH_3, **57**)	(ESI) calcd for $C_{26}H_{21}NO_3S$ [M^+ + H]: 428.1320; found: 428.1315
60b	7.94 (d, ^3J = 8.3 Hz, 1 H), 7.87 (s, 1 H), 7.72 (d, ^3J = 8.5 Hz, 1 H), 7.60 (ddd, ^3J = 8.3, 7.9 Hz, ^4J = 1.3 Hz, 1 H), 7.49–7.41 (m, 2 H), 6.74 (d, ^3J = 8.5 Hz, 2 H), 5.43 (d, ^4J = 1.1 Hz, 2 H), 3.62 (s, 6 H)	169.6 ($C_{q/CO}$), 158.1 ($C_{q/Ar}$), 140.2 ($C_{q/Ar}$), 136.2 ($C_{q/Ar}$), 135.4 ($C_{q/Ar}$), 132.8 ($C_{q/Ar}$), 130.3 (CH_{Ar}), 128.3 (CH_{Ar}), 128.2 (CH_{Ar}), 127.7 (CH_{Ar}), 126.3 (CH_{Ar}), 121.3 ($C_{q/Ar}$), 120.1 (CH_{Ar}), 111.8 ($C_{q/Ar}$), 104.1 (CH_{Ar}), 68.2 (CH_2), 55.9 (CH_3)	(EI) calcd for $C_{20}H_{16}O_4$ [M^+]: 320.1048; found: 320.1049
60c	7.98 (d, ^3J = 8.3 Hz, 1 H), 7.92 (s, 1 H), 7.65 (dd, ^3J = 8.1, 7.0 Hz, 1 H), 7.58 (d, ^3J = 8.3 Hz, 1 H), 7.45 (dd, ^3J = 8.1, 7.0 Hz, 1 H), 7.04 (s, 2 H), 2.40 (s, 3 H), 1.80 (s, 6 H)	169.5 ($C_{q/CO}$), 141.4 ($C_{q/Ar}$), 140.2 ($C_{q/Ar}$), 137.5 ($C_{q/Ar}$), 136.3 ($C_{q/Ar}$), 135.8 ($C_{q/Ar}$), 132.3 ($C_{q/Ar}$), 131.0 ($C_{q/Ar}$), 128.8 (CH_{Ar}), 128.3 (CH_{Ar}), 128.2 (CH_{Ar}), 127.0 (CH_{Ar}), 126.9 (CH_{Ar}), 120.4 ($C_{q/Ar}$), 120.0 (CH_{Ar}), 68.4 (CH_2), 21.3 (CH_3), 20.1 (CH_3)	(EI) calcd for $C_{21}H_{18}O_2$ [M^+]: 302.1307; found: 302.1307
60d	7.84 (d, ^3J = 7.9 Hz, 1 H), 7.73–7.70 (m, 1 H), 7.59–7.44 (m, 5 H), 7.41–7.35 (m, 1 H), 7.28–7.25 (m, 2 H), 4.54 (t, ^3J = 5.5 Hz, 2 H), 3.24 (t, ^3J = 5.5 Hz, 2 H)	145.5 ($C_{q/Ar}$), 138.8 ($C_{q/Ar}$), 134.92 ($C_{q/Ar}$), 134.87 ($C_{q/Ar}$), 132.6 ($C_{q/Ar}$), 130.9 (CH_{Ar}), 129.1 (CH_{Ar}), 128.8 (CH_{Ar}), 128.5 (CH_{Ar}), 128.3 (CH_{Ar}), 127.9 (CH_{Ar}), 127.3 (CH_{Ar}), 127.2 (CH_{Ar}), 126.2 (CH_{Ar}), 125.3 (CH_{Ar}), 121.5 ($C_{q/Ar}$), 66.9 (CH_2), 29.7 (CH_2)	(EI) calcd for $C_{19}H_{14}O_2$ [M^+]: 274.0994; found: 274.0994

Table 5 Analytical Data of New Compounds (continued)

Compound	^{1}H NMR (300 MHz, $CDCl_3$): δ	^{13}C NMR (75.5 MHz, $CDCl_3$): δ	HRMS: *m/z*
61b	8.75 (s, 1 H), 8.00–7.96 (m, 1 H), 7.54–7.43 (m, 6 H), 7.27–7.23 (m, 2 H), 4.45 (t, ^3J = 6.0 Hz, 2 H), 2.88 (t, ^3J = 6.0 Hz, 2 H)	166.0 ($C_{q/CO}$), 137.4 ($C_{q/Ar}$), 137.3 ($C_{q/Ar}$), 134.9 ($C_{q/Ar}$), 132.2 (CH_{Ar}), 131.9 ($C_{q/Ar}$), 130.0 (CH_{Ar}), 129.7 (CH_{Ar}), 128.9 (CH_{Ar}), 128.7 (CH_{Ar}), 127.8 (CH_{Ar}), 126.3 (CH_{Ar}), 122.8 ($C_{q/Ar}$), 60.4 (CH_2), 26.8 (CH_2)	(EI) calcd for $C_{19}H_{14}O_2$ [M^+]: 274.0994; found: 274.0993
60e	7.84–7.81 (m, 1 H), 7.70 (s, 1 H), 7.57–7.52 (m, 2 H), 7.43–7.36 (m, 2 H), 6.73 (d, ^3J = 8.3 Hz, 2 H), 4.51 (t, ^3J = 5.3 Hz, 2 H), 3.62 (s, 6 H), 3.23 (t, ^3J = 5.3 Hz, 2 H)	163.6 ($C_{q/CO}$), 157.4 ($C_{q/Ar}$), 138.5 ($C_{q/Ar}$), 135.0 ($C_{q/Ar}$), 134.9 ($C_{q/Ar}$), 132.3 ($C_{q/Ar}$), 129.2 (CH_{Ar}), 128.2 (CH_{Ar}), 127.6 (CH_{Ar}), 127.3 (CH_{Ar}), 126.0 (CH_{Ar}), 125.2 (CH_{Ar}), 122.9 ($C_{q/Ar}$), 116.1 ($C_{q/Ar}$), 104.3 (CH_{Ar}), 67.0 (CH_2), 55.9 (CH_3), 29.8 (CH_2)	(EI) calcd for $C_{21}H_{18}O_4$ [M^+]: 334.1205; found: 334.1205
69a/70a	8.14 (s, 1 H, **69a**), 8.03–7.97 (m, 1 H), 7.88 (s, 1 H, **70a**), 7.85 (s, 2 H), 7.71–7.65 (m, 2 H), 7.55–7.50 (m, 2 H), 7.49–7.47 (m, 1 H), 7.45–7.44 (m, 2 H), 7.44–7.41 (m, 2 H), 7.40–7.39 (m, 1 H), 7.38–7.36 (m, 1 H), 7.36–7.30 (m, 3 H), 7.25–7.23 (m, 1 H), 7.04 (br s, 1 H, NH, **70a**), 5.81 (br s, 1 H, NH, **69a**), 4.51 (s, 2 H, CH_2, **70a**), 4.25 (d, ^3J = 5.3 Hz, 2 H, CH_2, **69a**)	185.4 ($C_{q/CO}$), 149.4 (CH_{Ar}), 139.5 ($C_{q/Ar}$), 138.6 (CH_{Ar}), 135.1 (CH_{Ar}), 133.1 (CH_{Ar}), 132.6 (CH_{Ar}), 131.7 (CH_{Ar}), 130.6 ($C_{q/Ar}$), 130.0 ($C_{q/Ar}$), 129.6 ($C_{q/Ar}$), 128.7 ($C_{q/Ar}$), 128.6 (CH_{Ar}), 128.3 (CH_{Ar}), 127.9 (CH_{Ar}), 127.7 (CH_{Ar}), 127.5 (CH_{Ar}), 127.2 ($C_{q/Ar}$), 126.1 (CH_{Ar}), 125.6 ($C_{q/Ar}$), 125.0($C_{q/Ar}$), 121.6 (CH_{Ar}), 48.1 (CH_2, **69a**), 44.3 (CH_2, **70a**)	(EI) calcd for $C_{18}H_{13}NO$ [M^+]: 259.0997; found: 259.0997

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