HETEROCYCLES, Vol. 65, No. 9, 2005, pp. 2221 - 2257
Received, 14th June, 2005, Accepted, 25th July, 2005, Published online, 26th July, 2005

# PHOTOCHEMICAL ADDITION REACTIONS INVOLVING PHTHALIMIDES

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Abstract – This review summarizes photochemical addition reactions involving the phthalimide system from the pioneering work of Y. Kanaoka in the early 1970'ies to recent developments. Photoadditions of arenes, alkenes, alcohols, ethers, amines, thioethers, carboxylates and α-trialkylsilylmethyl-substituted compounds are described.

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## 1 INTRODUCTION

Since the pioneering work of Kanaoka and coworkers on the photochemistry of the phthalimide system,[1] a variety of applications in terms of synthetic organic photochemistry have been developed. Various aspects of the photochemistry of phthalimides have been reviewed over the last 25 years,[2] but a precise summary on *intermolecular* addition reactions was missing so far. With respect to recent developments and further mechanistic insights, we would like to add a comprehensive description of the scope and limitations of these reactions.

## 2 PHOTOPHYSICAL AND ELECTROCHEMICAL PROPERTIES OF PHTHALIMIDES

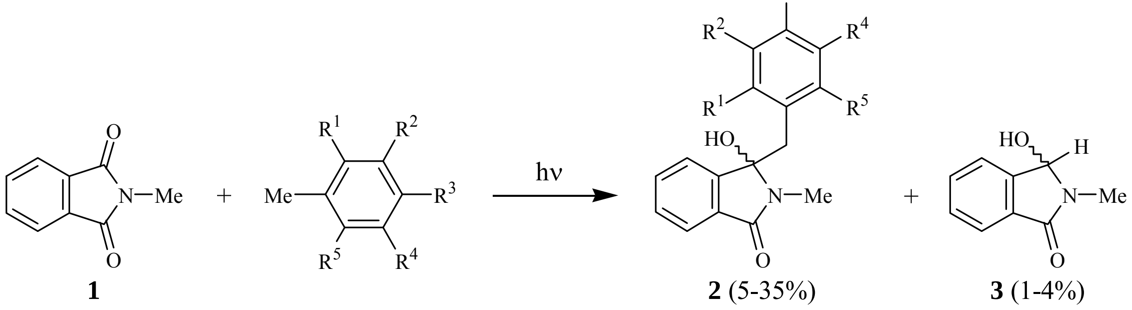
The photophysical[3] and electrochemical[4] properties of phthalimides have been intensively studied. In acetonitrile, *N*-alkylphthalimides show relatively simple UV absorption spectra with absorption maxima around 235 nm ($\pi,\pi^*$) and 290 nm ($n,\pi^*$), respectively.[3a] At room temperature, they furthermore exhibit weak fluorescence with low quantum yields ($\Phi_f < 1\times10^{-3}$) in ethanol or acetonitrile.[3b] Under oxygen free conditions, *N*-alkylphthalimides show a broad structureless phosphorescence centred around 450 nm with quantum yields between $\Phi_p = 0.4\text{-}0.7$ and triplet lifetimes between $\tau_p = 0.7\text{-}1.04$ s (at -196°C, in alcohol).[3a-c] The order of the excited states of phthalimides has been controversially discussed. The level of the ($n,\pi$) triplet state is either slightly below or above the lowest singlet state which accounts for the high intersystem crossing rates.

*N*-Methylphthalimide (**1**) is reversibly reduced to the corresponding radical anion at *ca.* -1.35 V in DMF,[4a,b] and at *ca.* -1.5 V in acetonitrile (*vs.* SCE),[4b] respectively. The presence of hydrogen donor sites in the side chain has a dramatic effect on the redox properties.[5] In particular, anodically shifted pre-waves emerge in the cyclic voltammograms which have been assigned to *intra-* and *intermolecular* hydrogen bonds to the phthalimide electrophore.

Due to their favorable photophysical and electrochemical properties, phthalimides are superior substrates for photoinduced electron transfer (PET) reactions.[5a-c] The limiting maximum oxidation potential of the electron donor depends on the excited state of the phthalimide electron acceptor,[3a] and can be estimated by the Rehm-Weller equation.[6] If the first excited singlet state is involved (**1**: $E_{00} = 3.8$ eV), the limiting oxidizing power for an isoenergetic electron transfer is *ca.* 2.4 V (*vs.* SCE). For the first excited triplet state (**1**: $E_{00} = 3.1$ eV), the limiting oxidizing power decreases to *ca.* 1.7 V (*vs.* SCE). In cases where the spectrocopically non-detectable second triplet state is populated (**1**: $E_{00} \approx 3.6$ eV), the oxidizing power increases by about 0.5 V.

## 3 PHOTOADDITIONS OF ARENES

It has been reported by Kanaoka *et al.* that a series of toluene derivatives add to electronically excited *N*-methylphthalimide (**1**) to give the corresponding addition products (**2**) in poor to moderate yields (Scheme 1; Table 1).[7] The best result was obtained for *p*-xylene with 35%, and a primary hydrogen abstraction from the benzylic position was postulated as crucial key-step. In all cases, the phthalimide was irradiated in the aromatic solvent and larger amounts of unreactive *N*-methylphthalimide were recovered. Due to a competing photoreduction reaction, the hydroxyphthalimide (**3**) was additionally isolated in low yields.

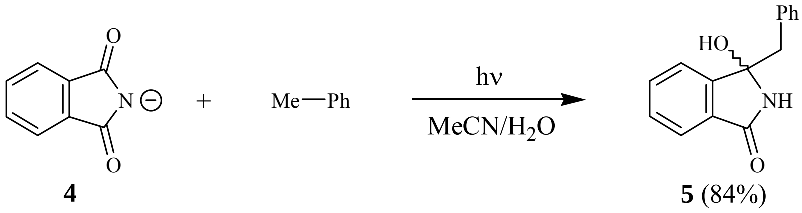


**Scheme 1**

**Table 1** Product composition for photoadditions of toluene derivatives to *N*-methylphthalimide (**1**).

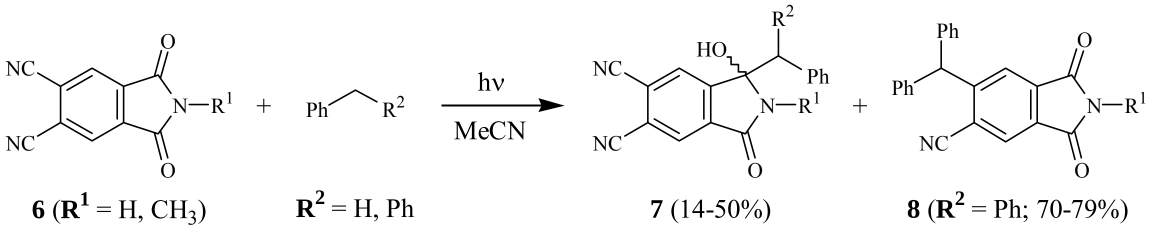
| Arene | | | | | Conversion | Composition | |
|---|---|---|---|---|---|---|---|
| **R$^1$** | **R$^2$** | **R$^3$** | **R$^4$** | **R$^5$** | **1** [%] | **2 [%]** | **3 [%]** |
| H | H | H | H | H | 30 | 5 | 2 |
| Me | H | H | H | H | 79 | 23 | 3 |
| H | Me | H | H | H | 59 | 7 | 2 |
| H | H | Me | H | H | 58 | 35 | 4 |
| H | Me | H | Me | H | 67 | 24 | 1 |

In contrast to **1**, the phthalimide anion (**4**) readily reacted with toluene to give the corresponding addition product (**5**) in 84% yield without any further side-products (Scheme 2).[8] In the absence of base, no conversion was achieved. Based on these findings, Suau and coworkers suggested an electron transfer mechanism between the anion and the *free* phthalimide prior to hydrogen abstraction from the aromatic side-chain and radical combination.



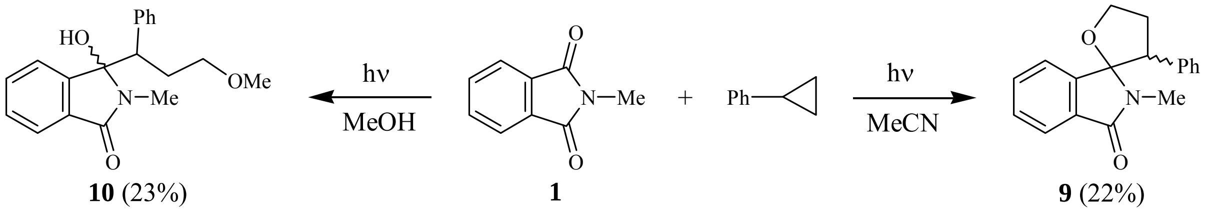
**Scheme 2**

In 1993, Albini *et al.* postulated an alternative electron transfer pathway.[9] The efficiency *via* this electron transfer route could be significantly enhanced for cyano-substituted phthalimides (**6**) as the electron transfer step became more exergonic. Most remarkably, substitution of the cyano-group (→ **8**) was observed beside addition to the carbonyl-position (→ **7**) when diphenylmethane (**R$^2$** = Ph) was used as the toluene derivative (Scheme 3).[9] The latter process was rationalized on the basis of an *in-cage* versus *out-of-cage* scenario.



**Scheme 3**

Another solvent depending, *intermolecular* addition reaction involving phenylcyclopropane as the electron donor was recently reported by Mazzocchi and coworkers.[10] Irradiation of *N*-methylphthalimide (**1**) in acetonitrile in the presence of phenylcyclopropane afforded a 1:1 mixture of isomeric *spiro*-tetrahydrofuranyllactams (**9**) in 22% yield. When the photolysis was performed in methanol, solvent-incorporated addition to produce **10** took place instead (Scheme 4). *Intramolecular* versions of these PET reactions have also been described.[10c]



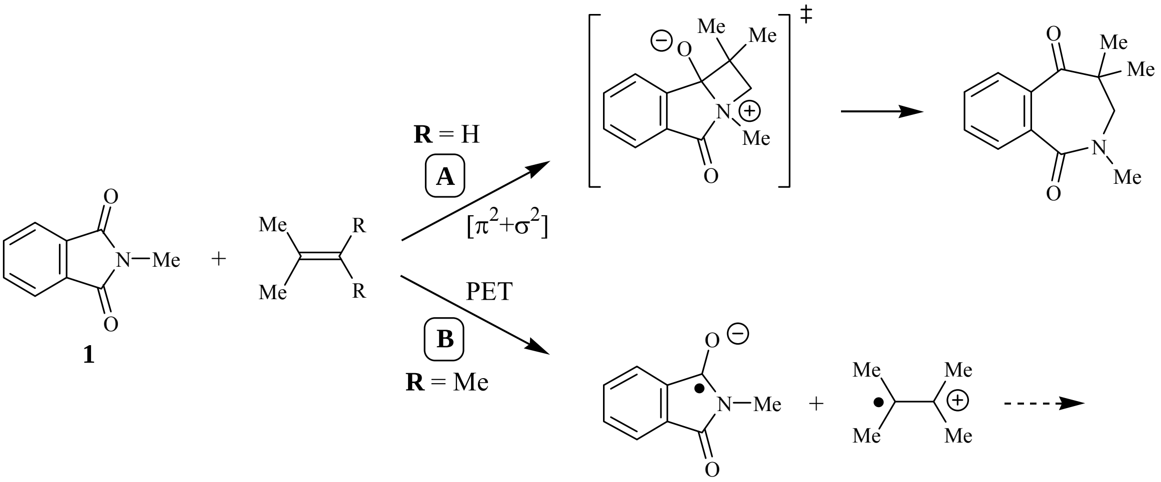
**Scheme 4**

## 4 PHOTOADDITIONS OF ALKENES

Photoadditions of alkenes to phthalimides are dominated by five major processes, and although mixtures are commonly obtained, we will highlight each of these processes individually:[1,2]

1. $[\pi^2+\sigma^2]$ Addition to the C(O)-N bond and formation of ring expanded benzazepinediones
2. Electron transfer leading to photoreduction to the corresponding carbinols
3. Electron transfer to the corresponding radical ion pair which is trapped by alcohols
4. Cycloaddition to the carbonyl bond and formation of oxetanes
5. Cycloaddition to the aromatic ring and formation of [4+2] photocycloaddition products.

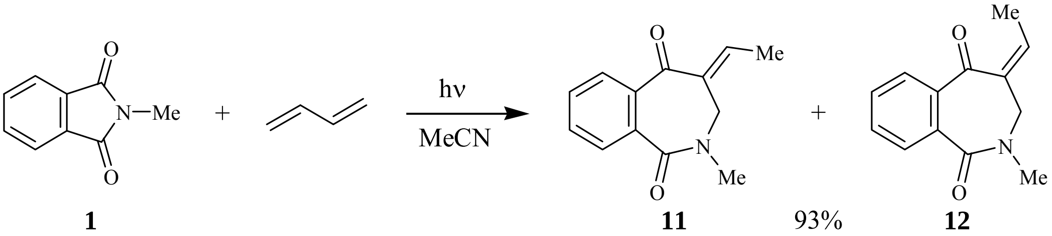
Generally speaking, the outcome of photoreactions of phthalimides with alkenes is dictated by the irradiation conditions and the oxidation potential of the C=C double bond in particular, and numerous studies have been reported independently by the groups of Mazzocchi[11] and Kubo over the last decades.[12] The feasibility of an electron transfer process between the alkene and the phthalimide can be estimated from the Rehm-Weller equation.[6] In cases where an electron transfer was *endergonic* with $\Delta G_{ET}$ >5 kcal/mol, $[\pi^2+\sigma^2]$ addition reactions to benzazepinediones were observed (Scheme 5; path **A**). When the electron transfer became more and more exergonic, electron transfer started to dominate (Scheme 5; path **B**). In the presence of suitable nucleophiles, *e.g.* alcohols, the intermediary formed radical ionic pair was trapped in an *anti*-Markovnikov fashion. In the absence of suitable trapping agents, back electron transfer, regenerating the starting materials, efficiently competed with proton transfer and radical combination to carbinols (*vide infra*). In cases where the ET was only slightly endergonic, both pathways competed and mixtures of $[\pi^2+\sigma^2]$ addition and PET products were obtained.



Scheme 5

## 4.1 Formation of benzazepinediones

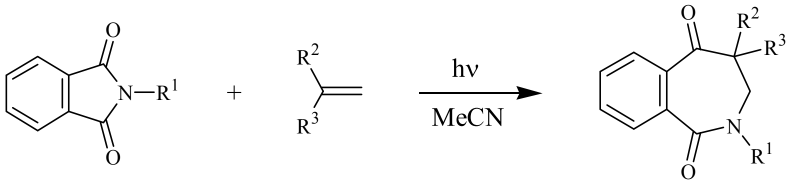
During quenching studies on *N*-alkylphthalimides with *cis*-piperylene, Mazzocchi and coworkers noticed that the phthalimide was reacting efficiently with the quencher. In order to avoid complications from competing *intra*- and *intermolecular* processes, the simplified model system *N*-methylphthalimide (**1**) and butadiene was irradiated in acetonitrile (Scheme 6).[13] The resulting products, which were obtained in a 93% yield based on recovered starting material, were identified as the isomeric benzazepinediones (**11**) and (**12**) formed *via* a [$\pi^2+\sigma^2$] photocycloaddition. The **11**/**12** ratio varied with irradiation conditions and compound (**12**) readily isomerized to the more stable isomer (**11**). Similarly, the reaction occurred with isoprene and 1,3-pentadiene and the corresponding products were isolated in yields of 49% (2 isomers) and 50%. Remarkably, the diene always added in a *regiospecific* manner to **1** with its terminal carbon attached to the nitrogen. In contrast, no product formation was observed with cyclopentadiene and 2,5-dimethyl-2,4-hexadiene, or when **1** was replaced with *N*-phenylphthalimide or phthalimide, respectively.[13]



Scheme 6

In 1978, Maruyama and Kubo reported a detailed photoaddition study of various alkenes to either *N*-methylphthalimide (**1**) or phthalimide (**13**).[14] The corresponding benzazepinediones (**14**) were isolated in fair to good yields of 25-67% when *ca.* 3 equivalents of the alkene were used (Scheme 7; Table 2). With

2-methy-1-pentene (**R**$^2$ = Me, **R**$^3$ = Pr) or 1-pentene (**R**$^2$ = H, **R**$^3$ = Pr), the primary photoproducts underwent instant Norrish-II cleavages of the propyl substituents.



**1**/**13** **14** (25-67%)

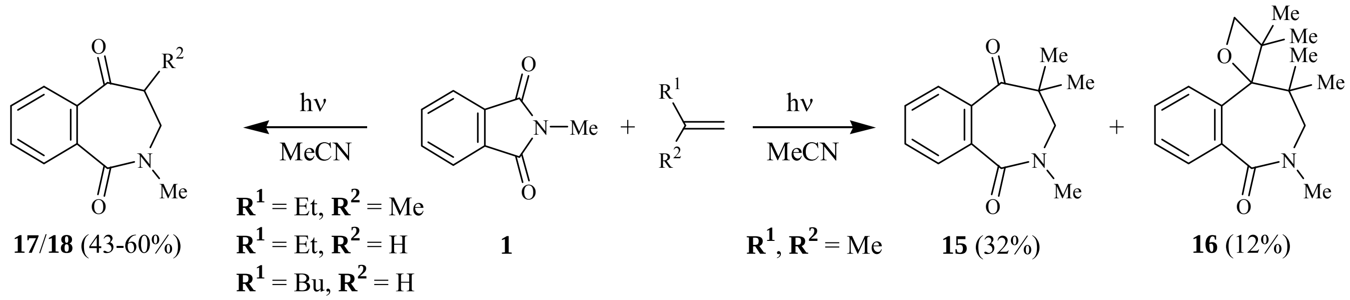
**Scheme 7**

**Table 2** Product composition for photoadditions of alkenes to phthalimides (**1**) and (**13**).

| Phthalimide | Alkene | | **14** | | | |
|---|---|---|---|---|---|---|
| **R**$^1$ | **R**$^2$ | **R**$^3$ | **R**$^1$ | **R**$^2$ | **R**$^3$ | yield [%] |
| Me (**1**) | Me | Me | Me | Me | Me | 67 |
| Me (**1**) | Me | Pr | Me | Me | H[a] | 42 |
| Me (**1**) | H | Pr | Me | H | H[a] | 25 |
| Me (**1**) | H | Ph | Me | H | Ph | 37 |
| Me (**1**) | Me | Ph | Me | Me | Ph | 40 |
| H (**13**) | H | Ph | H | H | Ph | 32 |
| H (**13**) | Me | Ph | H | Me | Ph | 41 |

[a] Norrish-II cleavages of the propyl substituents

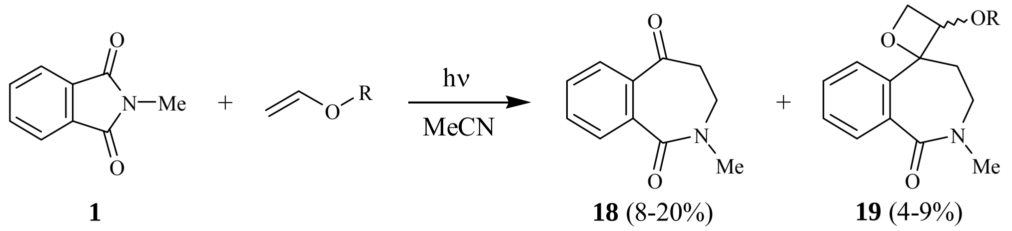
In the same year, Mazzocchi *et al.* published similar results on this application.[15] In contrast to Maruyama's and Kubo's work, *N*-methylphthalimide (**1**) was irradiated in the presence of fifty equivalents of alkene. As a result, photolysis of **1** and 2-methylpropene (**R**$^1$, **R**$^2$ = Me) in acetonitrile furnished the benzazepinedione (**15**) together with its oxetane derivative (**16**) in yields of 32% and 12% (Scheme 8). **16** was formed from **15** *via* a secondary Paternò-Büchi reaction. 2-Methyl-1-butene (**R**$^1$ = Et, **R**$^2$ = Me) gave the benzazepinedione (**17**; **R**$^2$ = Me) through a sequence of photoaddition and Norrish-II cleavage. Likewise, 1-butene (**R**$^1$ = Et, **R**$^2$ = H) and 1-hexene (**R**$^1$ = Bu, **R**$^2$ = H) yielded the parent, unsubstituted benzazepinedione (**18**; **R**$^2$ = H) in yields of 60% and 46% (Scheme 8), respectively.



**Scheme 8**

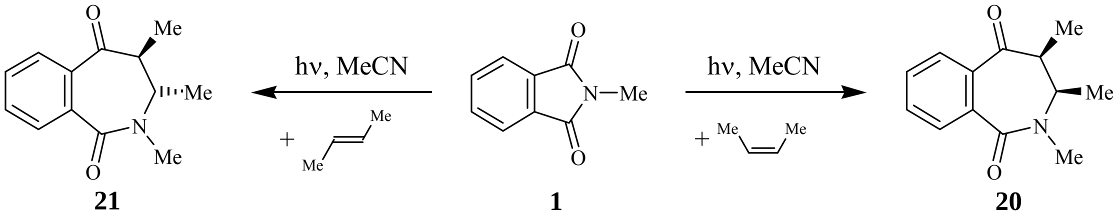
In contrast, no products were observed for 2-methyl-2-butene, 2-methyl-2-pentene or 2,3-dimethyl-2-butene, respectively. The latter olefin solely gave a small amount (5%) of the photoreduced *N*-methylphthalimidine (**103**) (*vide infra*). This differing behavior was striking and was associated with the oxidation potentials of the alkenes. Mazzocchi concluded that a *non*-productive electron transfer quenching was occurring with alkenes having low oxidation potentials (Scheme 5; *vide supra*).[11,15] In an extension of this work, Mazzocchi *et al.* studied a larger variety of different olefins, and the authors noted that benzazepinedione formation generally occurred with 1-substituted, 1,1-disubstituted and 1,2-disubstituted alkenes. While there were few examples of benzazepinedione formation with *tri*-substituted alkenes, no addition products were observed with *tetra*-substituted or cyclic ones.[16] In the latter cases, *N*-methylphthalimide (**1**) tended to undergo photoreduction with these compounds instead (*vide infra*).

On irradiation of *N*-methylphthalimide (**1**) with a fifty-fold excess of either ethyl vinyl ether (**R** = Et) or *n*-butyl vinyl ether (**R** = Bu) in acetonitrile, Mazzocchi and coworkers found that the vinyl ethers reacted in a similar manner as alkenes, yielding the benzazepinediones (**18**) in low yields of 8% and 20% (Scheme 9).[17] Subsequent Paternò-Büchi reaction to **18** furthermore furnished the corresponding oxetanes (**19**) in 9% and 4% yield. Decomposition products arising from a primary Paternò-Büchi reaction to **1** were also obtained in small amounts (*vide infra*). In contrast, isopropenyl ethyl ether and 1,1-dimethoxyethylene showed no reaction.



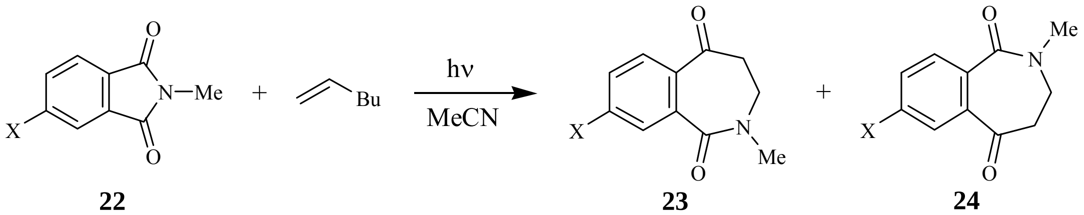
**Scheme 9**

In order to prove the mechanism for the photoaddition reaction, *N*-methylphthalimide (**1**) was reacted with either *cis*- or *trans*-2-butene. To avoid epimerization or interference *via* a slow *cis*/*trans*-isomerization of the alkene, the reaction was stopped at low conversion rates. Following this strategy, the corresponding benzazepinediones (**20**) and (**21**) were formed in stereoselectivities >95% (Scheme 10).[18] Based on these findings, a concerted [$\pi^2+\sigma^2$] cycloaddition through a dipolar intermediate or alternatively an addition through a biradical with hindered rotation around the C-C bond has been favored.



Scheme 10

To further prove the mechanistic scenario, Mazzocchi and coworkers studied the regioselectivity of the cycloaddition for unsymmetrically substituted phthalimides.[19] In line with other know photochemical reactions at that time,[20] the authors predicted that donor substituents would preferentially direct the incoming alkene to the *meta* position, whereas acceptor groups would direct to the *para* position. Consequently, a series of unsymmetrically substituted phthalimides (**22**) were irradiated in the presence of 1-hexene in acetonitrile and the dealkylated products (**23**) and (**24**) arising from a secondary Norrish type-II cleavage were isolated (Scheme 11; Table 3). As correctly predicted, the methoxyphthalimide derivative (**22**; **X** = MeO) exclusively gave the *para* product (**23**) in a yield of 32%. Other donor substituents still slightly favored the formation of the *para* product (**23**), whereas the strong accepting carboxymethyl group (**22**; **X** = $CO_2Me$) preferentially gave the *meta* product (**24**). The results were inconsistent with those of a proven radical anion trapping mechanism, through which only single regioisomers were obtained (*vide infra*), and thus, a concerted reaction pathway was postulated.

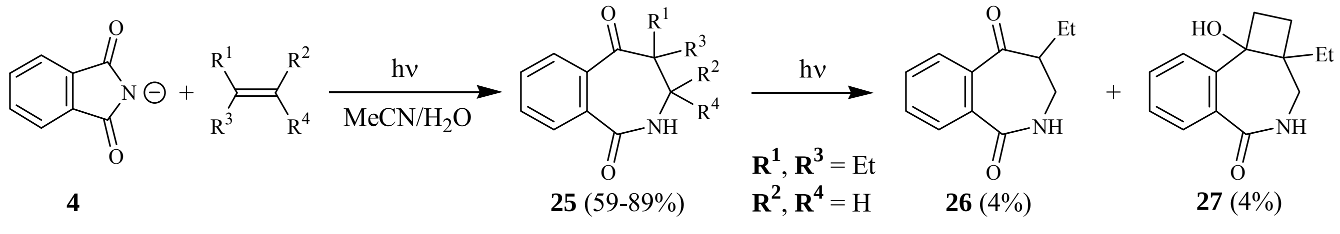


Scheme 11

**Table 3** Photoadditions of 1-hexene to unsymmetrically substituted phthalimides (**22**).

| **22**<br>X | Yield<br>**23** + **24** [%] | Composition<br>**23** [%] | <br>**24** [%] |
|---|---|---|---|
| MeO | 32 | 100 | — |
| Me | 32 | 57 | 43 |
| Cl | 45 | 52 | 48 |
| $CO_2Me$ | 46 | 27 | 46 |

Recently, Suau and coworkers reported that benzazepinediones were formed during the irradiation of the phthalimide anion (**4**) in the presence of alkenes.[21] To circumvent reaction with the solvent, the originally applied alcohols were replaced by a 7:1 mixture of acetonitrile and water. The outcome of the reaction was, however, sensitive to the concentration of the base and best results were obtained at [phthalimide] > [$HO^-$]. Applying these conditions, photolysis of **4** with either cyclopentene, cyclohexene, 2,3-dimethyl-2-butene or 2-ethyl-1-butene gave the respective photocycloaddition products (**25**) in good to excellent yields of 59-89% based on conversion (Scheme 12; Table 4). Most remarkably, these alkenes had previously failed to give benzazepinediones with both, *free* phthalimide and *N*-methylphthalimide.[11,13] This differing behavior was associated with the low reduction potential of **4** and the efficient quenching of its fluorescence by alkenes. In case of 2-ethyl-1-butene (**R**$^1$, **R**$^3$ = Et, **R**$^2$, **R**$^4$ = H), the primary photoproduct partially underwent Norrish-II cleavage to **26** and Yang-cyclization to **27**.[21b] The photocycloaddition of phthalimide also worked with alkenylbenzenes and the corresponding products (**25**) were found with highly regioselectivity and moderate to excellent yields of 41-86% based on conversions (Table 4).[21b]



**Scheme 12**

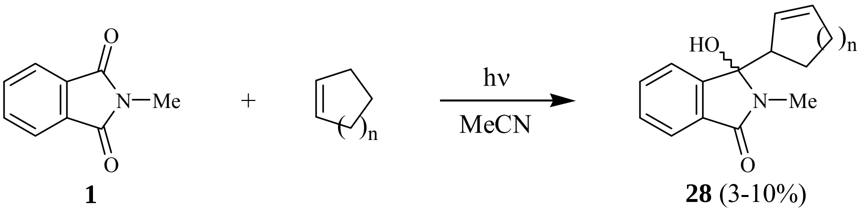
**Table 4** Photoadditions of alkenes to the phthalimide anion (**4**).

| Alkene | | | | Conversion | Yield |
|---|---|---|---|---|---|
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | **4** [%] | **25** [%] |
| $(CH_2)_3$ | | H | H | 80 | 86[a] |
| $(CH_2)_4$ | | H | H | 90 | 89[a] |
| Me | Me | Me | Me | 85 | 84[a] |
| Et | H | Et | H | 85 | 59[b] |
| Ph | H | H | H | 92 | 90[a] |
| Ph | H | H | Me | 88 | 72[a] |
| Ph | Me | H | H | 93 | 68[a] |
| 4-$MeOC_6H_4$ | H | H | H | 74 | 41[c] |
| 3,4-$(OCH_2O)C_6H_3$ | H | H | Me | 28 | 51[c] |
| Ph | H | Ph | H | 20 | 78[c] |

Phthalimide/NaOH ratios: [a] 1:1.5 – [b] 1:1.2 – [c] 3.4:1.

## 4.2 Photoreductions

In 1974, Kanaoka and Hatanaka briefly reported the earliest examples of photoadditions of alkenes to phthalimides.[22] Photolysis of *N*-methylphthalimde (**1**) with either cyclopentene or cyclohexene in acetonitrile furnished the corresponding addition products (**28**) in low yields of 3% and 10% (Scheme 13), respectively. The authors noted particularly that no oxetane was detected from a competing Paternò-Büchi reaction. The reaction of **1** with cyclohexene was subsequently confirmed by Mazzocchi and coworkers in 1978.[15]

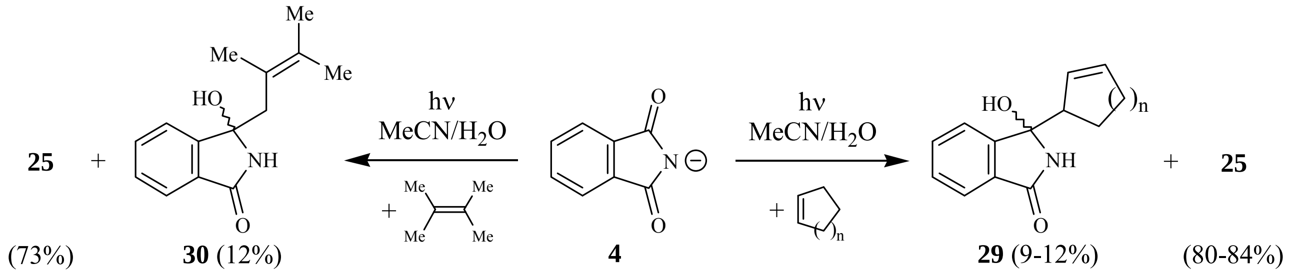


**1**

**28** (3-10%)

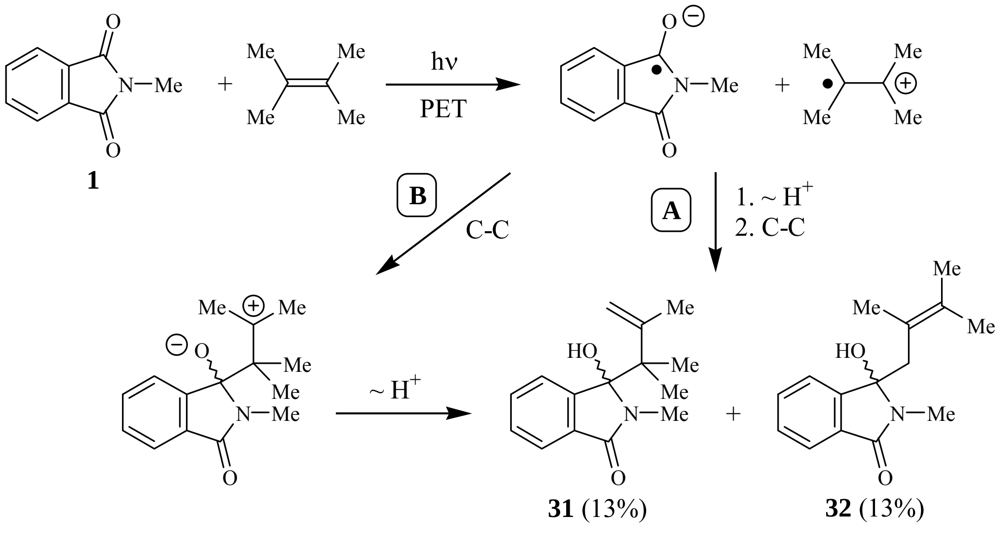
**Scheme 13**

Likewise, cyclohexene underwent a similar reaction with *N*-ethylphthalimide in methanol and gave, besides 27% of the corresponding methanol-trapping product (*vide infra*), the photoreduced product (similar to **28**; n = 2) in 25% yield. The reaction was postulated to proceed through the triplet ($T_1$) state.[3c] Similarly, photoreduction products (**29** and **30**) were isolated in minor amounts of 9-12% during irradiations of the phthalimide anion (**4**) with either cyclopentene, cyclohexene or 2,3-dimethyl-2-butene, when a pH of 10 was kept or the ratio of phthalimide to NaOH was set to 1:1.2 (Scheme 14), respectively.[21b] In contrast, 2-ethyl-1-butene failed to give any carbinols under these conditions. Main products in all cases were the benzazepinediones (**25**;*vide supra*).



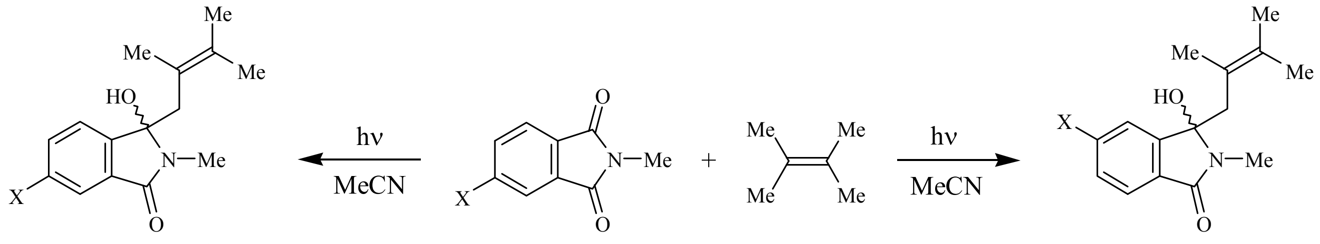
**Scheme 14**

Mazzocchi and Klinger studied extensively the photoreaction of *N*-methylphthalimde (**1**) with 2,3-dimethyl-2-butene in acetonitrile.[11b] Prolonged irradiation was necessary to obtain high conversion rates and a pair of the photoreduction products (**31**) and (**32**) was isolated in equal yields of 13% each (Scheme 15). Furthermore, a third product was obtained in 4% yield, which was identified as an oxetane from a competing Paternò-Büchi reaction (*vide infra*). The authors suggested an initial electron transfer as key-step in the mechanistic scenario. As noticeable from the required irradiation time, back electron transfer regenerating the starting materials competed efficiently with follow-up reactions. To account for the equal amounts of carbinols (**31**) and (**32**) formed, two competing proton transfer and radical combination pathways were postulated. *Intermolecular* proton transfer and radical combination (path **A**) yields the isomeric pair, whereas radical combination and *intramolecular* proton transfer furnishes compound (**31**) exclusively (path **B**). Sensitization and quenching studies with indanone and fluorene suggested that the carbinol products arise from the singlet state of **1**,[11b] and not from the triplet state as was previously suggested.[3c]



**Scheme 15**

The regiochemistry of the photoreduction was examined by Mazzocchi and coworkers for unsymmetrically substituted *N*-methylphthalimides (**22**).[23,19b] Upon irradiation in acetonitrile and trapping of the initial radical anion with 2,3-dimethyl-2-butene (Scheme 16) it was found that electron-accepting groups (**R** = $CO_2Me$) direct the incoming substituent in the predicted *para*-manner (→ **33**), while electron-donating groups (**R** = Me, Cl, OMe) gave the corresponding *meta*-products (**34**; *meta* and *para* with respect to the reduced carbonyl group). Remarkably, only one regioisomer was formed although yields were not given. In comparison to related regioselectivity studies in methanol (*vide infra*),[24] the authors suggested that the directing effect of the aryl substituent is more clearly manifested in the aprotic solvent acetonitrile.

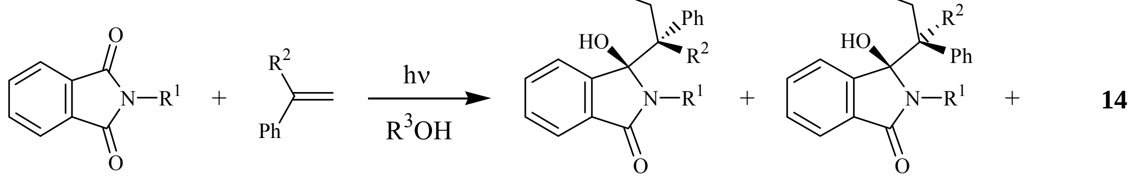


**33** (**X** = $CO_2Me$) **22** **34** (X = MeO, Me, Cl)

Scheme 16

## 4.3 Alcohol incorporations

Maruyama and Kubo reported that irradiation of *N*-methylphthalimide (**1**), phthalimide (**13**) or *N*-acetoxymethylphthalimide (**35**) in alcoholic solvents with various alkenylbenzenes gave the diastereoisomeric solvent incorporated addition products (**36**) and (**37**) in yields up to 83% based on conversion of 10-15% (Scheme 17; Table 5).[12b,25] In cases where methanol was replaced by other alcohols, the corresponding benzazepinedione (**14**) was additionally obtained *via* a competing [$\pi^2$+$\sigma^2$] addition in yields up to 30%. The authors explained this effect by a decrease in solvent polarity when going from methanol to *tert*-butanol. Later, Mazzocchi and coworkers demonstrated that the efficiency of the trapping reaction was furthermore dependent on the nucleophilicity of the solvent.[26]



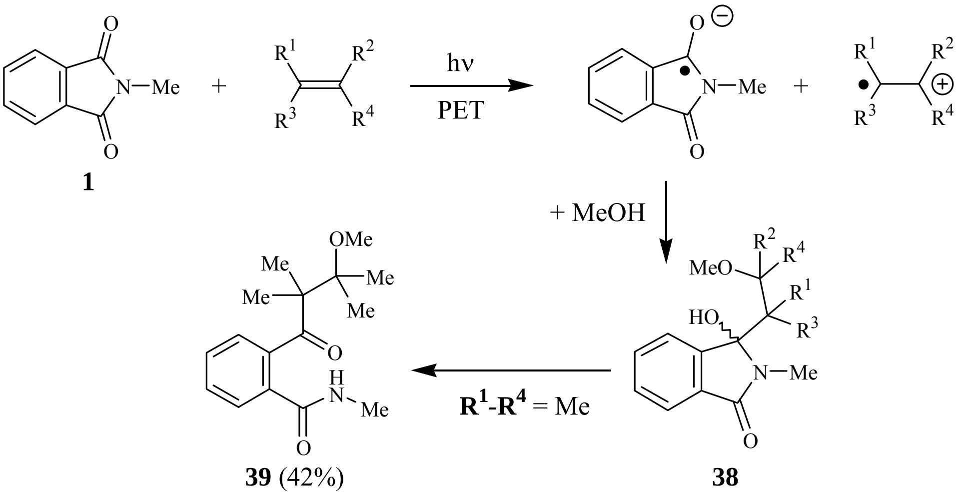
**1**/**13**/**35** **36** (28-40%) **37** (25-34%) (trace-30%)

Scheme 17

**Table 5** Solvent incorporative photoadditions of alkenylbenzenes to phthalimides (**1**, **13** and **35**).

| Phthalimide<br>$R^1$ | Olefin<br>$R^2$ | Alcohol<br>$R^3$ | Yields<br>**36** [%] | <br>**37** [%] | <br>**14** [%] |
|---|---|---|---|---|---|
| Me (**1**) | H | Me | 40 | 34 | — |
| Me (**1**) | H | Et | 38 | 31 | trace |
| Me (**1**) | H | *i*-Pr | 32 | 25 | 18 |
| Me (**1**) | H | *t*-Bu | 28 | 26 | 30 |
| Me (**1**) | Me | Me | 40 | 30 | — |
| Me (**1**) | Me | Et | 29 | 16 | 11 |
| Me (**1**) | Ph | Me | 83 | | — |
| H (**13**) | H | Me | 39 | 30 | — |
| H (**13**) | H | Et | 32 | 22 | 13 |
| H (**13**) | Me | Me | 40 | 35 | trace |
| H (**13**) | Me | Et | 37 | 34 | 8 |
| H (**13**) | Me | *i*-Pr | 16 | 16 | 30 |
| $CH_2OAc$ (**35**) | H | Me | 32 | 32 | 30 |

As stated earlier (*vide supra*), photoadditions of aliphatic olefins were sensitive to the number of alkyl substituents and thus the oxidation potential of the C=C double bond.[11,12] Therefore, the groups of Mazzocchi[27] and Kubo[25] independently examined photoreactions of *N*-methylphthalimide (**1**) with a variety of alkenes in methanol. In general, the methanol incorporated adducts were obtained by the reaction of olefins possessing at least two alkyl substituents and the corresponding solvent incorporated addition products (**38**) were obtained in yields of 15-52% (Scheme 18; Table 6). For unsymmetrically substituted alkenes, products (**38**) were formed as diastereoisomeric mixtures. Remarkably, the photoproduct arising from 2,3-dimethyl-2-butene ($\mathbf{R^1}$-$\mathbf{R^4}$ = Me) underwent ring-opening to **39**. Disubstituted olefins additionally gave [$\pi^2+\sigma^2$] addition products (**14**) due to their high oxidation potentials (*vide supra*).



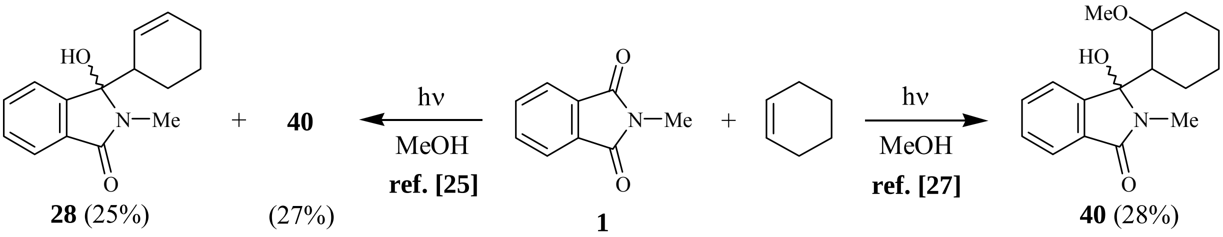
Scheme 18

**Table 6** Solvent incorporative photoadditions of aliphatic alkenes to *N*-methylphthalimide (**1**).

| Alkene | | | | Yields | |
|---|---|---|---|---|---|
| **R¹** | **R²** | **R³** | **R⁴** | **38**[a] [%] | **14** [%] |
| Me | H | Me | H | 18[b]/15[c] | 50[b]/57[c] |
| Me | Me | H | H | 15[c] | 57[c] |
| Me | Me | Me | H | 52[b]/41[c] | — |
| Me | Me | Me | Me | 42 (**39**)[c] | — |

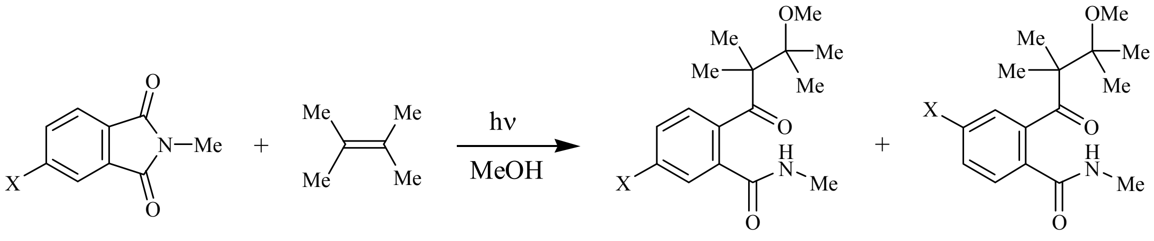
[a] Diastereoselectivity neglicted for clarity. [b] Kubo and Maruyama.[25] [c] Mazzocchi and coworkers.[27]

Somewhat contradictory results were reported for the photoaddition in methanol involving cyclohexene (Scheme 19). According to Mazzocchi *et al.* this photoreaction gave exclusively a diastereoisomeric mixture of the corresponding trapping products (**40**) in 28% yield,[27] whereas Kubo and Maruyama isolated the photoreduction product (**28**; n = 2) in a yield of 25%, next to 27% of **40** (diastereoisomeric mixture).[25] Likewise, *N*-ethylphthalimide furnished a mixture of solvent-trapping (similar to **40**; 27%) and photoreduction product (similar to **28**; 25%) when irradiated in methanol solution.[3c]



Scheme 19

The regioselectivity of the solvent-incorporating photoaddition has been studied by Mazzocchi and Khachik for unsymmetrically substituted phthalimides (**22**) and 2,3-dimethyl-2-butene in methanol (Scheme 20; Table 7).[24] In line with their related regioselectivity studies on the photoreduction and the [$\pi^2$+$\sigma^2$] addition (*vide supra*) the authors expected radical ion formation at the imide carbonyl *para* to an acceptor and *meta* to a donor group. Indeed the donor substituted methoxyphthalimide (**22**; **X** = MeO) predominantly gave the *meta* product (**42**), although in a 34:66 mixture with its *para* regioisomer (**41**). Other donor containing phthalimides behaved similarly, while the only product acquired for the strongly accepting carboxymethyl-group (**X** = $CO_2Me$) was the *para* regioisomer (**41**). Yields were, however, not given by the authors.



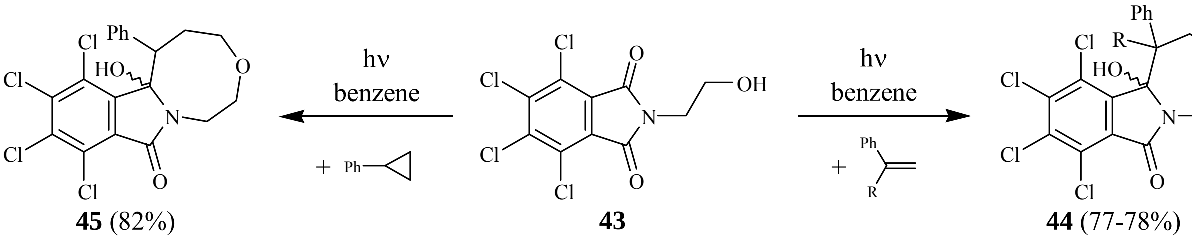
**22** **41** **42**

**Scheme 20**

**Table 7** Photoadditions of 2,3-dimethyl-2-butene to unsymmetrically substituted phthalimides (**22**).

| 22 | Composition | |
|---|---|---|
| X | **41** [%] | **42** [%] |
| MeO | 34 | 66 |
| Me | 55 | 45 |
| Cl | 56 | 44 |
| $CO_2Me$ | 100 | — |

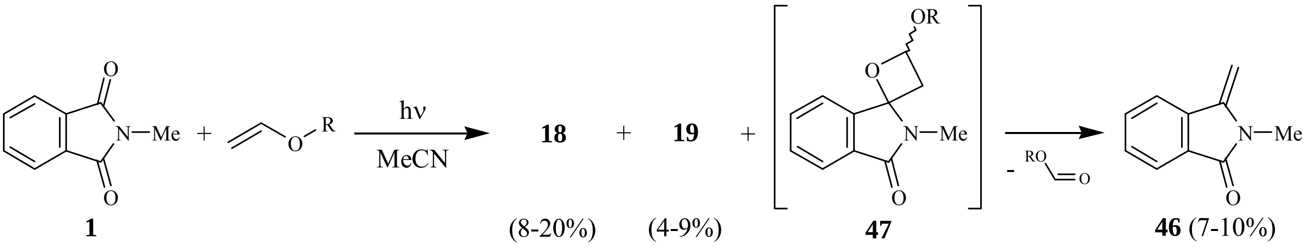
Recently, Xue *et al.* described an interesting modification using tetrachlorophthalimides with remote hydroxyalkyl substituents.[28] During photolysis in the presence of alkenes and in benzene, the alkene radical cation intermediate was trapped by the terminal hydroxy function, followed by an *intramolecular* radical-radical combination to give medium to macrocyclic compounds. For example, irradiation of *N*-(2-hydroxyethyl)-4,5,6,7-tetrachlorophthalimide (**43**) with 1,1-diphenylethylene (**R** = Ph) or α-methylstyrene (**R** = Me) gave the seven-membered ring products (**44**) in yields of 77% and 78% (Scheme 21), respectively. Likewise, phenylcyclopropane gave the eight-membered ring system (**45**) in 82% yield. In contrast, the corresponding *N*-(2-hydroxyalkyl)phthalimides were almost photostable when reacted with alkenes under identical conditions.



**Scheme 21**

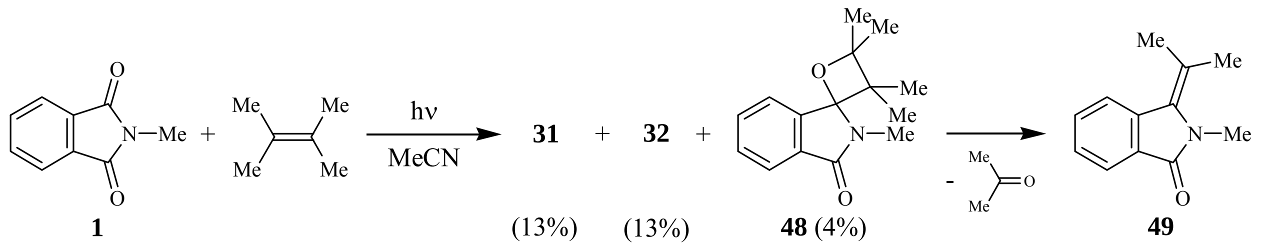
## 4.5 Paternò-Büchi reactions

Paternò-Büchi reactions of phthalimides are rather rare and occur as minor side-reactions with alkenes. In 1978, Mazzocchi and coworkers reported on the reaction of ethyl and *n*-butyl vinyl ethers with *N*-methylphthalimide (**1**).[17] Beside the benzazepinediones (**18**) and its subsequent Paternò-Büchi product (**19**; *vide supra*), the authors isolated small amounts of 3-methylene-isoindolone (**46**) (Scheme 22), a decomposition product of the primary formed oxetanes (**47**).



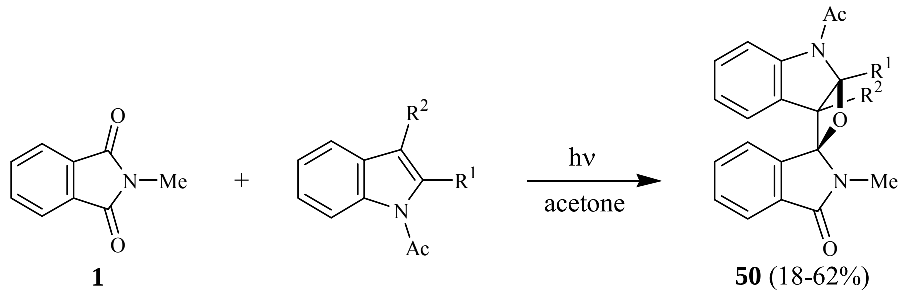
**Scheme 22**

A few years later, Mazzocchi *et al.* finally succeeded in the isolation of an *intermolecularly* formed oxetane.[11b,29] Irradiation of an acetonitrile solution of *N*-methylphthalimide (**1**) and 2,3-dimethy-2-butene resulted in the formation of the isomeric photoreduction products (**31**) and (**32**) (*vide supra*), together with the Paternò-Büchi product (**48**) in a 4% yield (Scheme 23). The yield of **48** increased with increasing olefin concentration. In chloroform, the oxetane (**48**) readily decayed to acetone and **49**. Sensitization and quenching experiments showed that **48** originated from the triplet state of **1**, whereas photoreduction to **31** and **32** occurred *via* the singlet state. In a similar manner, when **1** was irradiated in the presence of α-methylstyrene, the Paternò-Büchi product (analogous to **48**) was again isolated in a yield of 4% together with 21% of its isomeric decomposition products (similar to **49**) and the corresponding benzazepinedione (**14**; 60%).[29] In contrast, photolysis of **1** in the presence of 1,1-diphenylethene gave a mixture of the benzazepinedione (**14**; $\mathbf{R^1}$, $\mathbf{R^2}$ = Ph; 11%) and the decomposition analogue of **49** (10%), together with a dimerization product of the initial alkene.[12]



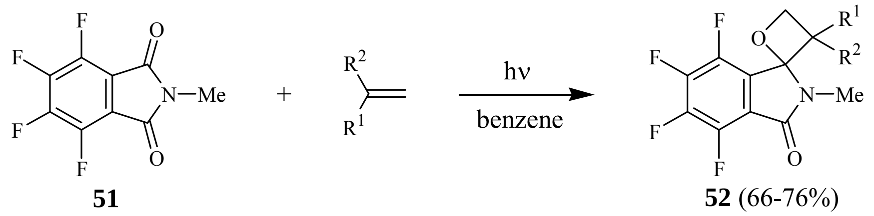
Scheme 23

In contrast, irradiations of **1** in acetone and in the presence of 2- and 3-substituted *N*-acylindol derivatives furnished the sterically hindered oxetanes (**50**) in moderate yields of 18-62% (Scheme 24).[30] In some cases, the isolated products were sensitive towards column chromatography on alumina and underwent ring-opening reactions.



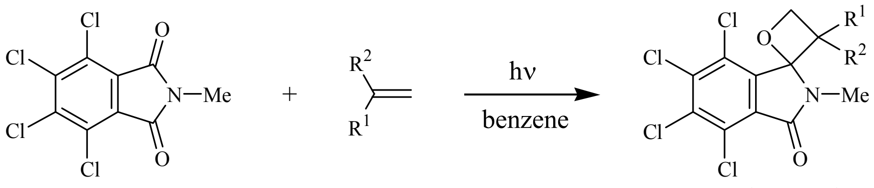
Scheme 24

As reported by Kubo and Umehara, 4,5,6,7-tetrafluoro-*N*-methylphthalimide (**51**) exclusively gave oxetanes (**52**) in yields of 66-68% when irradiated in benzene solutions with either styrene, α-methylstyrene or 1,1-diphenylethylene (Scheme 25), respectively.[31] With styrene and α-methylstyrene diastereoisomeric mixtures were obtained. In contrast, photolysis in methanol gave exclusively the expected alcohol incorporation products (similar to **36** and **37**).



Scheme 25

Likewise, irradiations of 4,5,6,7-tetrachloro-*N*-methylphthalimide (**53**) in the presence of various styrene derivatives gave the diastereoisomeric spirooxetanes (**54**) as main products in yields of 67-91% based on conversion (Scheme 26).[32] With *p*-methylstyrene and α-methylstyrene, the corresponding benzazepinediones (similar to **14**) were obtained as side-products in 31% and 12% yield, respectively, whereas indene additionally furnished smaller amounts (17%) of its diastereoisomeric photoreduction product (analogous to **28**).

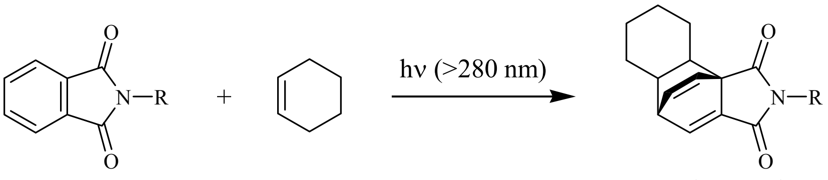


**53** **54** (67-91%)

**Scheme 26**

## 4.6 *Ortho*- and *para*-cycloadditions

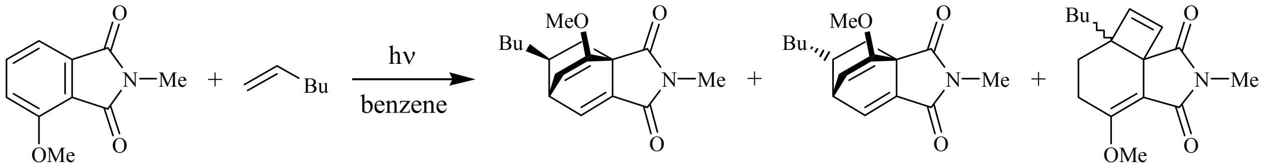
Examples of [4+2] *para*-photocycloaddition reactions at the benzene moiety of the phthalimide have been reported by Schwack, who examined the irradiation ($\lambda > 280$ nm) of the fungicide *N*-trichloromethylthiophthalimide (**55**; **R** = $SCCl_3$) in cyclohexene.[33] Along with the expected carbinol (similar to **28**; 80%) and oxetane (analogue to **48**; 6%), an unexpected third product was isolated in 11% yield, which he identified as the *para*-cycloadduct (**56**) (Scheme 27). Similar *para*-cycloadducts were isolated exclusively from *N*-methylphthalimide (**1**) and *N*-phenylphthalimide (**57**; **R** = Ph) in yield of 44% and 90%, respectively, but these products were found to be mixtures of three different isomers.[33]



**1/55/57** **56** (11-90%)

**Scheme 27**

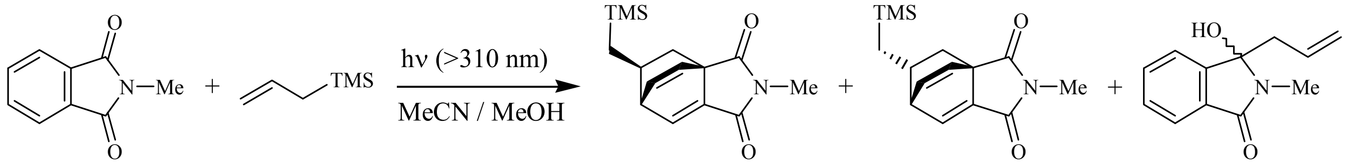
Suau and coworkers reported that the addition of 1-hexene to 3-methoxy-*N*-methylphthalimide (**58**) proceeded in a similar way when irradiated in benzene, giving two *para*-cycloaddition products (**59**) and (**60**), together with an *ortho*-cycloaddition product (**61**).[34] The epimers (**59**) and (**60**) were obtained in a 4:1 ratio (59%), while **61** was isolated in a yield of 25% (Scheme 28). The same photoproducts were also formed during irradiation in acetonitrile under identical conditions, although in slower rates.[34] The formation of the *para*-cycloaddition adducts (**59**) and (**60**) was rationalized on basis of an initial [2+2] photoaddition, followed by subsequent electrocyclic ring opening, photoinduced [1,7] sigmatropic rearrangement and ring closure.



**58** **59** (47%) **60** (12%) **61** (25 %)

**Scheme 28**

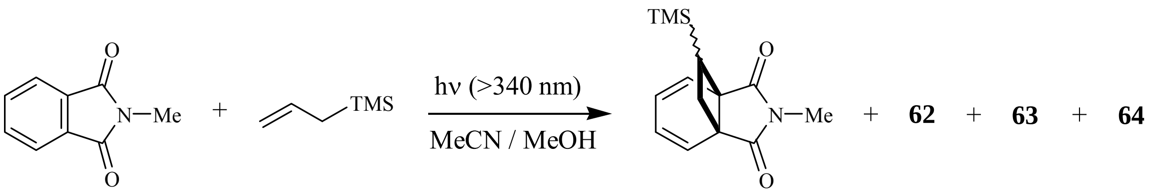
The irradiation ($\lambda > 310$ nm) of *N*-methylphthalimide (**1**) with allyltrimethylsilane in a mixture of acetonitrile and methanol (19:1) has been described by Kubo and coworkers.[35] Two stereoisomeric products (**62** and **63**) are formed in 37% and 17% yield, respectively, *via* a [4+2] *para*-cycloaddition reaction to the benzene moiety of **1**. Furthermore, the addition product (**64**) was obtained in a yield of 13% (Scheme 29). With increasing concentration of the silane, the yield of **64** increased steadily whereas the amounts of **62** and **63** decreased, although their stereoisomer ratios remained almost constant. Sensitization studies using indanone established that **62** and **63** are formed through the triplet state.[35]



**1** **62** (37%) **63** (17%) **64** (13%)

**Scheme 29**

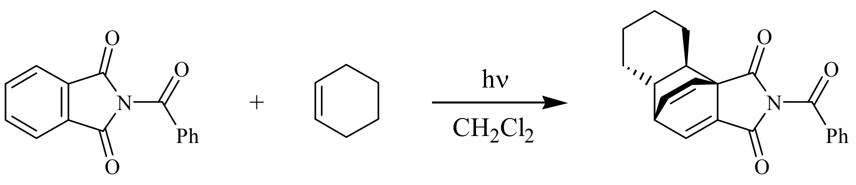
Irradiation at a longer wavelength ($\lambda > 340$ nm) of a solution of **1** and allyltrimethylsilane gave identical products as described above, but also a novel cycloadduct (**65**) arising from [2+2] addition at the benzene moiety of **1** (Scheme 30). Yields were not reported since the cycloadduct (**65**) was highly photoreactive and decomposed to **1** with increasing irradiation time.[35]



**1** **65**

**Scheme 30**

More recently, Howie and coworkers reported on the addition of cyclohexene to *N*-benzoylphthalimide (**66**) using dichloromethane as solvent. The *para*-cycloaddition product (**67**) was isolated in 80% yield based on a conversion of just *ca.* 5% (Scheme 31).[36a] Likewise, *N*-ethyltetrachlorophthalimide gave an analogous [4+2] *para*-cycloaddition product, although as a diastereoisomeric mixture.[36b] For *N*-acetyl-tetrachlorophthalimide, however, cleavage of the acetyl group occurred prior to *para*-cycloaddition.[36c]

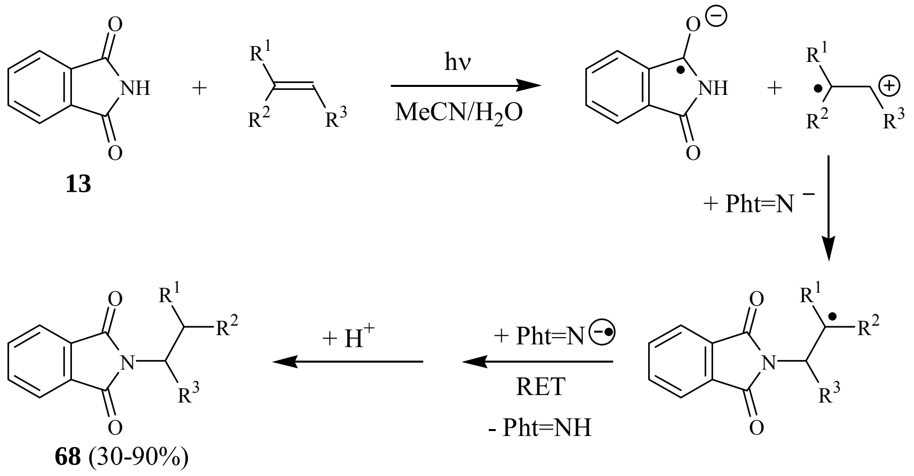


**66** **67** (80%)

**Scheme 31**

## 4.7 Phthalimidations

An interesting reaction of the phthalimide anion (**4**)/alkene system is the photochemical phthalimidation of unactivated double bonds.[37] The success of this application strongly depends on the $OH^-$ concentration. At $[OH^-] > [\text{phthalimide}]$, $[\pi^2+\sigma^2]$ addition to benzazepinediones (**25**) is predominantly observed (*vide supra*),[21] whereas at $[OH^-] < [\text{phthalimide}]$ photoaddition of phthalimide to the double bond of the alkene takes place. Using the latter conditions, *photophthalimidation* of cyclohexene and a series of styrene derivatives were examined by Suau and coworkers.[37] Irradiation of the olefins in the presence of excess phthalimide (**13**) and a small amount of NaOH gave the expected *photophthalimidation* products (**68**) in fair to excellent yields of 30-90%. (Scheme 32; Table 8). The use of a high concentration of **13** prevented absorption of light by the olefins and thus follow-up reactions of the *phthalimidation* products (**68**). In the mechanism proposed by the authors,[37] the phthalimide (**13**) acts as a sensitizer. Electron transfer from the olefin to the phthalimide singlet excited state produces the corresponding radical ion pair. The cation radical is trapped by the phthalimide anion (**4**) to give the most stable radical intermediate. Back electron transfer (BET), followed by protonation, yields the photoaddition products (**68**). The mechanism is consistent with the fact that no fluorescence was detected from the phthalimide anion at the phthalimide/hydroxide ion ration used, confirming that light is indeed absorbed by the phthalimide.



Scheme 32

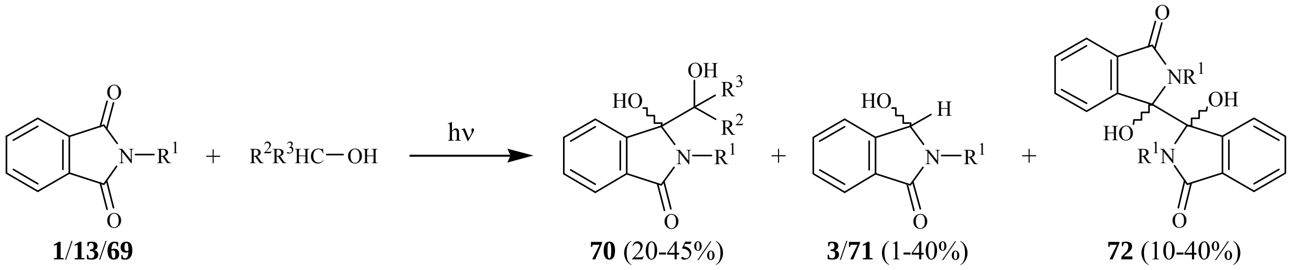
**Table 8** Photophthalimidation reactions involving phthalimide (**13**).

| Alkene<br>**$R^1$** | <br>**$R^2$** | <br>**$R^3$** | Conversion<br>olefin [%] | Yield<br>**68 [%]** |
|---|---|---|---|---|
| H | $(CH_2)_4$ | | 44 | 70 |
| Ph | H | H | 75 | 53 |
| Ph | Me | H | 80 | 90 |
| Ph | H | Me | 60 | 44 |
| Ph | H | Ph | 76 | 71 |
| Bn | H | H | 50 | 30 |
| 4-$MeOC_6H_4$ | H | H | 90 | 70 |
| 4-$MeOC_6H_4$ | H | Me | 76 | 60 |
| 3,4-$OCH_2OC_6H_3$ | H | Me | 71 | 51 |
| Indene | | | 75 | 90 |

## 5 PHOTOADDITIONS OF OXYGEN CONTAINING COMPOUNDS

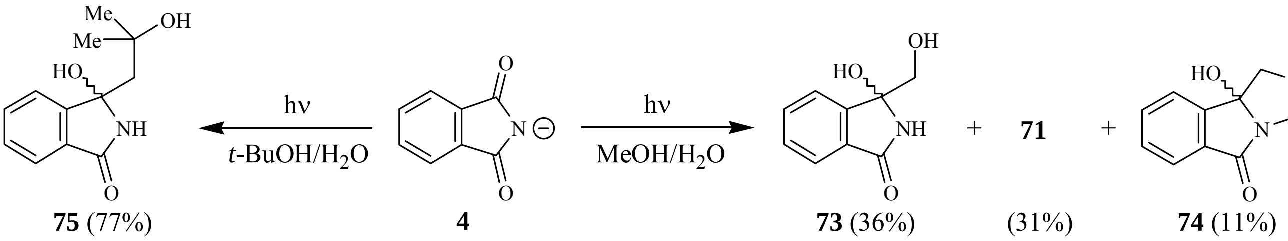
### 5.1 Photoadditions of alcohols

When alcohols are used as solvents in the irradiation of *N*-methylphthalimide (**1**), phthalimide (**13**) or *N*-ethylphthalimide (**69**), addition products (**70**) were obtained in low to moderate yields of 20-45% (Scheme 33).[38,39] Comparable amounts of hydroxyphthalimide (**3** and **71**) were isolated from competing photoreduction reactions. **13** additionally gave larger quantities of its corresponding dimerization product (**72**; **$R^1$** = H). In contrast, *N*-methylenebisphthalimides solely gave dimerization or photoreduction products when irradiated in isopropanol.[40] For all cases examined, the authors suggested that a free radical mechanism involving hydrogen transfer from the α-position of the alcohol was in operation.



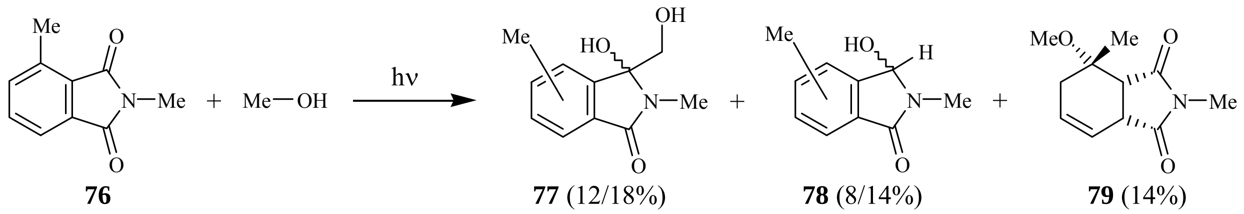
**Scheme 33**

In contrast to the free phthalimide, its anion (**4**) underwent efficient photoreactions with alcohols (Scheme 34).[8,21a] In aqueous methanol, the corresponding addition product (**73**) was isolated in 36% yield besides 31% of the primary reduction product (**71**; **R$^1$** = H). Additionally, the cyclic compound (**74**) was obtained in 11% yield and a follow-up reaction of (**73**) was postulated to explain its formation. The phthalimide anion was also reactive to *tert*-butanol and irradiation furnished the addition product (**75**) in a good yield of 77%. Remarkably, this compound was formed *via* a β-hydrogen abstraction from the alcohol. On the contrary, *N*-methylphthalimide (**1**) remained photostable when irradiated in *tert*-butanol.[8]



**Scheme 34**

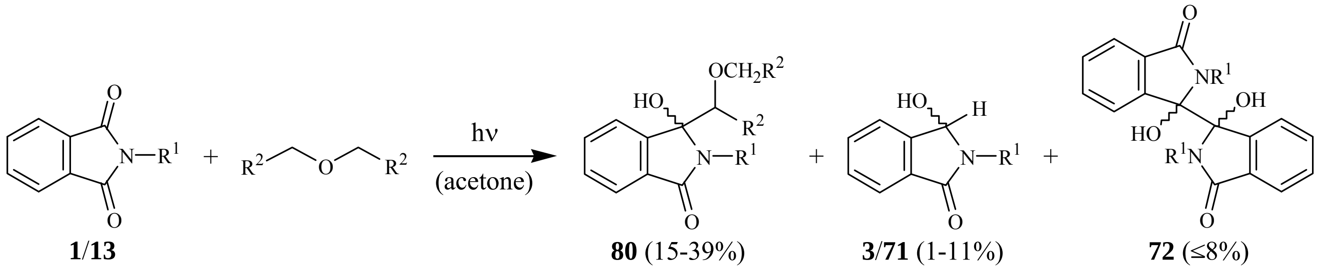
Irradiation of *N*,3-dimethylphthalimide (**76**) in methanol gave, besides two sets of isomeric photoreduction (**77**) and addition products (**78**), the dearomatized compound (**79**) as a single diastereoisomer (Scheme 35), which was apparently formed by a PET addition of the alcohol to the benzene moiety of the chromophore.[41] In ethanol and isopropanol, solely dearomatized products were obtained in yields of 27% and 31%, respectively. Likewise, *N*-methylphthalimide (**1**) and *N*,4-dimethylphthalimide underwent *photodearomatization* when irradiated in isopropanol.[41]



**Scheme 35**

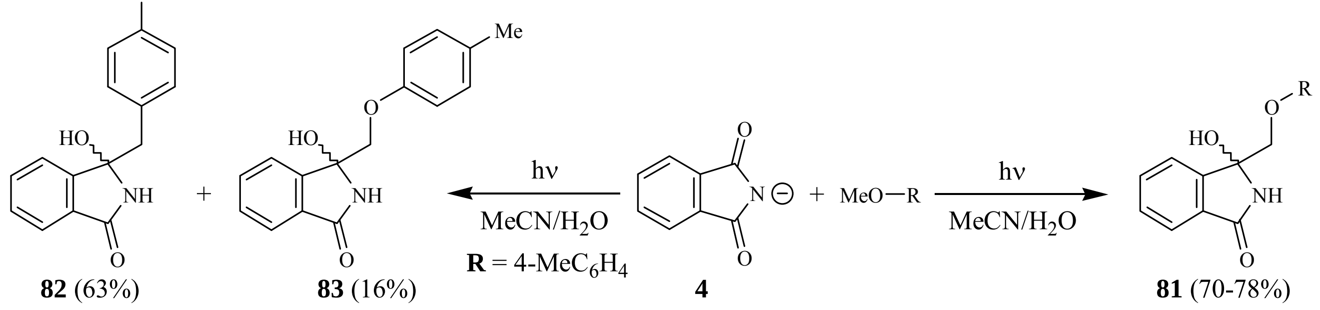
## 5.2 Photoadditions of ethers

Kanaoka[22] found that diethyl ether, THF and 1,4-dioxane added to *N*-methylphthalimde (**1**), while Roth[39,42] and Tanabe[43] independently reported on the photoadditions of ethers to phthalimide (**13**) and other *N*-substituted phthalimides. Acyclic (*e.g.* diethyl ether) as well as cyclic (*e.g.* THF, 1,4-dioxane) ethers gave the corresponding α-addition products (**80**) in moderate yields of 15-39% (Scheme 36). In some cases, minor amounts of the corresponding reduction (**3** and **71**) and dimerization (**72**) products were isolated, and these side reactions were especially pronounced for phthalimide (**13**). When acetone was used as dilutant, its trapping product (similar to **104**; *vide infra*) was furthermore isolated as a minor product in 5% for the phthalimide/dioxane pair.[42] *Thalidomide* solely underwent photoreduction in the presence of THF,[42] whereas the pesticide *Imidan* exclusively showed fragmentation of the side-chain when irradiated in diethylether.[43]



**Scheme 36**

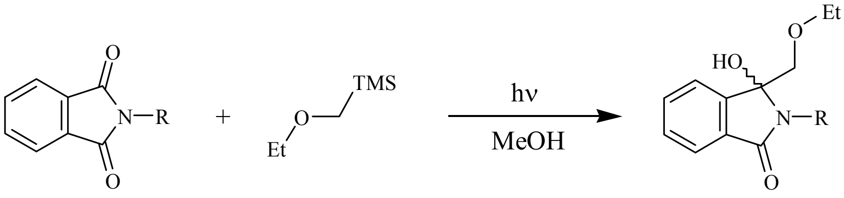
The efficiency of the photoaddition was dramatically improved for the phthalimide anion (**4**) and high yields of **81** of 70-78% were achieved (Scheme 37). Furthermore, the reaction proceeded in a highly selective manner without any side-products arising from photoreduction processes.[8] However, when other potent hydrogen donor sides were present as in 4-methoxytoluene, product mixtures arising from competing hydrogen abstraction from both methyl groups were obtained (Scheme 37).



**Scheme 37**

### 5.3 Photoadditions of α-trialkylsilylmethyl-substituted ethers

*Intra-* and *intermolecular* PET reactions of α-trialkylsilyl (TMS) methoxy-substituted phthalimides were developed by Yoon and Mariano.[44] The α-TMS group has a profound effect on the oxidation potential of the ether oxygen, which is lowered by about 0.5 V.[45] Consequently, electron transfer from the heteroatom to the electronically excited phthalimide becomes energetically feasible. The presence of the silyl group additionally enhances the efficiency and selectivity of the subsequent photoaddition. As an example, trimethylsilylmethyl ethyl ether yielded the corresponding addition products (**84**) in acceptable yields when irradiated in methanol (Scheme 38).[46] The photoreaction was, however, less efficient in acetonitrile where - in an extreme case - phthalimide (**13**) showed no reaction at all.

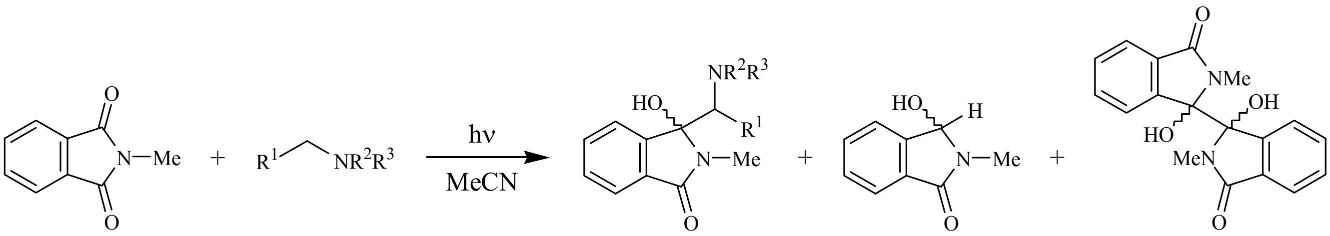


Scheme 38

## 6 PHOTOADDITIONS OF NITROGEN CONTAINING COMPOUNDS

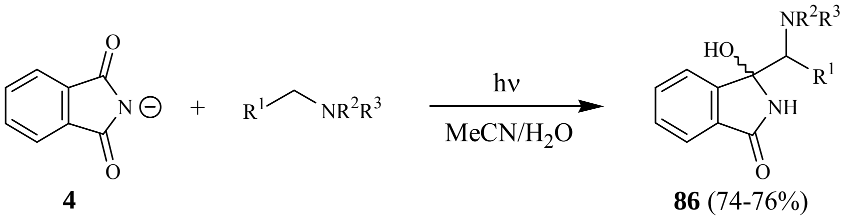
### 6.1 Photoadditions of amines

The addition of triethylamine, *N*,*N*-dimethylcyclohexane amine and *N*,*N*-dimethylaniline, which are efficient photoreducing agents for aromatic ketones,[47] to *N*-methylphthalimde (**1**) has been briefly reported by Kanaoka *et al.*,[7] affording the aminocarbinols (**85**) in low to moderate yields (Scheme 39). The photoadditions were, however, sensitive to the reaction conditions and in general proceeded rather sluggishly, and larger amounts of photoreduction (**3**) or dimerization products (**72**; $\mathbf{R^1}$ = Me) were observed.



Scheme 39

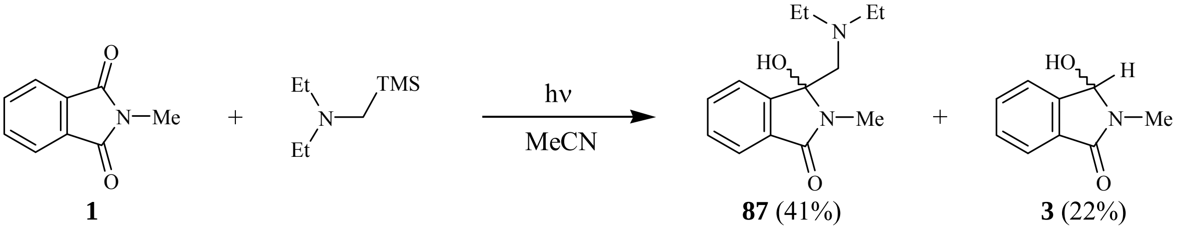
In line with other hydrogen donors (*vide supra*), the phthalimide anion (**4**) reacted readily and selectively with either triethylamine or *N*,*N*-dimethylaniline, and the corresponding addition products (**86**) became available in good yields of 74% and 76% (Scheme 40).[8]



Scheme 40

### 6.2 Photoadditions of α-trialkylsilylmethyl-substituted amines

Yoon and Mariano examined PET reactions of *N*-trimethylsilylmethyl-*N*,*N*-diethylamine with phthalimides.[46] The outcome of the photoaddition showed, however, a remarkable solvent dependency. In acetonitrile or dichloromethane, *N*-methylphthalimide (**1**) gave mixtures of the corresponding addition product (**87**) and the reduced hydroxyphthalimidine (**3**), whereas irradiations in methanol or *n*-hexane solely furnished **3** (Scheme 41). In sharp contrast, phthalimide (**13**) underwent reductive dimerization to **72** (**R$^1$** = H) in both, methanol and acetonitrile.[46]

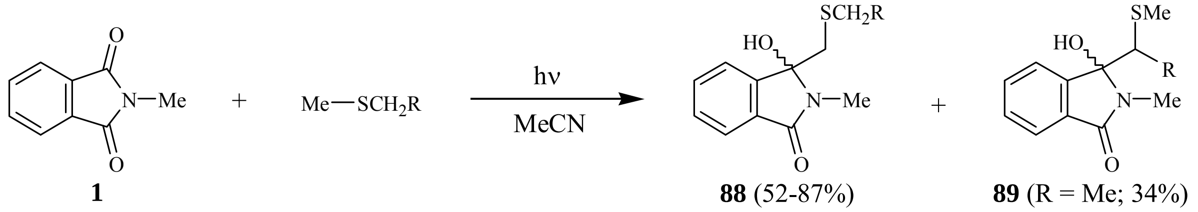


Scheme 41

## 7 PHOTOADDITIONS OF SULFUR CONTAINING COMPOUNDS

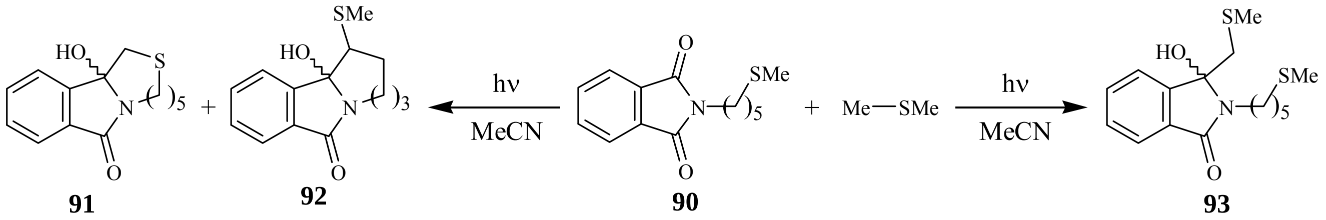
### 7.1 Photoadditions of thioethers

The photoaddition of some sulfides to *N*-methylphthalimide (**1**) has been described by Kanaoka and coworkers.[48] In methanol, acetone and acetonitrile, a 1:2 ratio of **1** to dimethyl sulfide gave **88** in 16, 69 and 80% (Scheme 42), respectively. The yield in acetone was increased to 79% if a 1:10 ratio of **1** *vs*. sulfide was used, while yields in acetonitrile were improved to 87% when a more powerful lamp was used. A 1:2 ratio of *N*-methylphthalimide and ethyl methyl sulfide in acetonitrile gave **88** in 52% yield, along with *threo*- and *erythro*-**89** in 19% and 15% yields (Scheme 42), respectively. The quantum yields of the product formation in acetonitrile were determined as Φ = 0.06 ($Me_2S$) and 0.05 (MeSEt), respectively.



**Scheme 42**

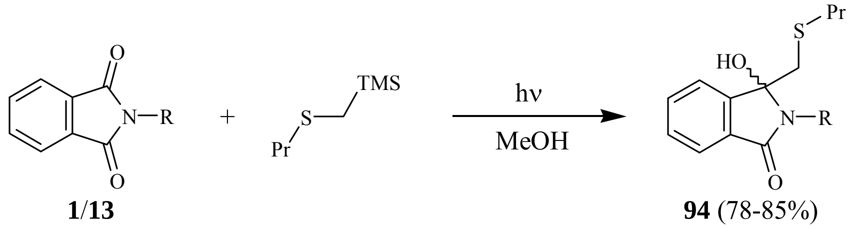
Irradiation of *N*-(5-methylthiopentyl)phthalimide (**90**), which was shown by the authors to undergo an *intramolecular* cyclization reaction to **91** and **92** in acetonitrile, in the presence of dimethyl sulfide afforded the addition product (**93**). By varying the concentration of dimethyl sulfide, the competition between the addition and cyclization reactions was also studied. The addition reaction was found to be competitive with the cyclization reaction only at dimethyl sulfide concentrations 10-times higher than that of **90** (Scheme 43).[48]



**Scheme 43**

### 7.2 Photoadditions of α-trialkylsilylmethyl-substituted thioethers

Yoon and Mariano described photoadditions of trimethylsilylmethyl *n*-propyl thioether with *N*-methylphthalimide (**1**) and phthalimide (**13**).[46] The corresponding products (**94**) were isolated in good yields of 78-85% when irradiated in methanol (Scheme 44). In acetonitrile, the reaction proceeded with much lower conversions and larger amounts of dehydration products were additionally obtained.

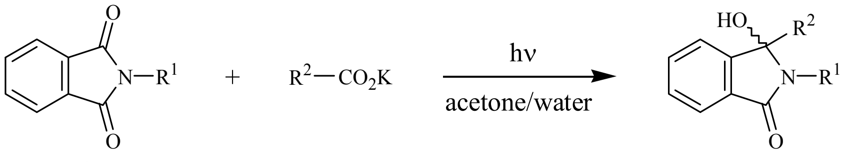


**Scheme 44**

# 8 PHOTOADDITIONS OF CARBOXYLATES

## 8.1 Photoadditions of alkyl carboxylates

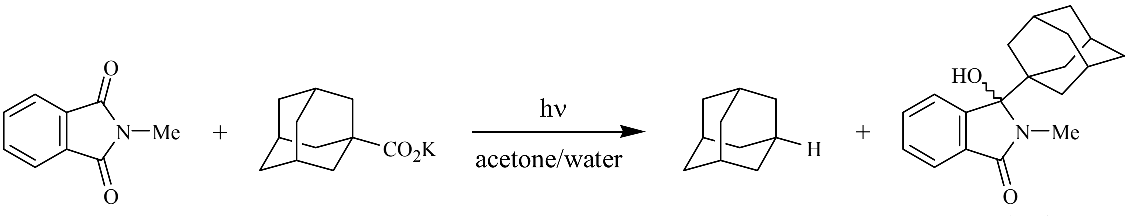
Griesbeck and coworkers have recently established the photodecarboxylation of ω-phthalimido carboxylates as a versatile strategy for the construction of medium to macrocyclic ring-systems.[49] Likewise, alkyl carboxylates underwent *intermolecular* addition reactions to the corresponding alkyl hydroxyphthalimidines (**95**) in good to excellent yields (Scheme 45).[50] The reaction was also applied to large multigram scales using a 308 nm XeCl excimer light source.[50b,51] Consequently, this method represents a mild and convenient alternative to thermal procedures, *e.g.* $SmI_2$-mediated coupling of organic halides ($SmI_2$/R-X),[52a] addition of organometallic compounds (R-Mg-X or R-Li),[52b-d] or alkylation with organic halides using lithium in liquid ammonia (Li/$NH_3$/R-X),[52e] respectively.



**1**/**56** **95** (39-89%)

Scheme 45

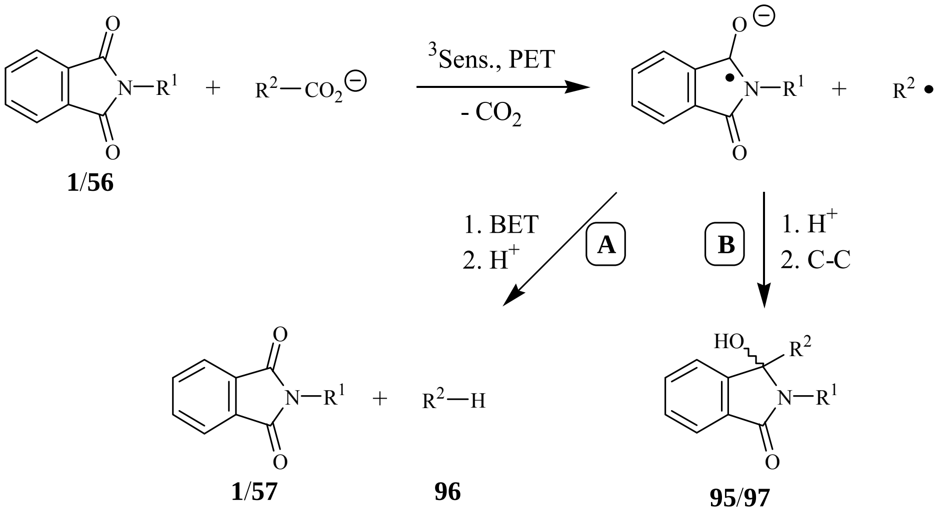
When the potassium salt of 1-adamantanecarboxylic acid was used the corresponding alkane adamantane (**96**) was isolated as main product in yields of 60-69% (Scheme 46). Most of the *N*-methylphthalimide (**1**) remained unchanged and could be reisolated. In one experiment the photoaddition product (**97**) was obtained in 2% yield.



**1** **96** (60-69%) **97** (2%)

Scheme 46

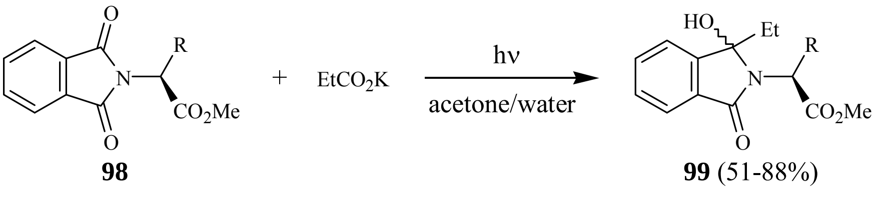
Although the oxidation potentials of carboxylates are relatively high compared to other electron donor groups (*e.g.* acetate: $E_{Ox.}$ = 1.54 V in MeCN, 2.65 V in $H_2O$ *vs.* SCE[53]), rapid *intramolecular* photoinduced electron transfer *via* the excited $^3\pi,\pi^*$ triplet state or the higher $^3n,\pi^*$ state has been proposed (Scheme 47).[54] Subsequent decarboxylation of the carboxy radical gives the terminal carbon radical. In case of 1-adamantanecarboxylic acid, back electron transfer (BET) generates the corresponding carbanion,[55] which is subsequently protonated by water (path **A**). For all other derivatives, protonation and biradical combination afforded the addition products (path **B**).



Scheme 47

A special case was the irradiation of **1** in the presence of sodium formate as the product composition was sensitive to the reaction conditions applied. Hence, the outcome of the irradiation was dominated by stepwise *photoreduction* or *photo-dearomatization*, and both pathways are known for phthalimides (*vide supra*)[7,41] and related imide chromophores.[56]

An interesting application for this remarkably efficient photoaddition was the highly *chemoselective* ethylation of *N*-phthaloylamino acid methyl esters (**98**).[50a] In all cases examined (Scheme 48), the *intermolecular* decarboxylative addition to **99** dominated and products arising from *intramolecular* hydrogen abstractions[57] were not observed. Unlike alternative nucleophilic additions (*e.g.* Grignard reaction[52b,c]), the photoinduced alkylation proceeded selectively at the imide carbonyl group and not the corresponding ester group. The diastereoselectivity for the ethyl transfer reaction was negligible to moderate (Table 9).[58]

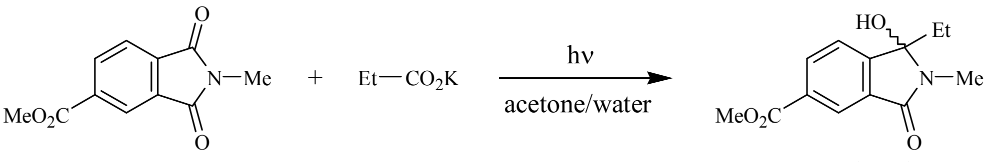


Scheme 48

**Table 9** Photodecarboxylative ethylation of *N*-phthaloylamino acid methyl esters (**98**).

| **98** | | **99** | |
|---|---|---|---|
| **R** | Amino acid | Yield [%] | *d.e.* [%] |
| H | Gly | 88 | — |
| Me | *L*-Ala | 89 | 4 |
| *i*-Pr | *L*-Val | 51 | 6 |
| *i*-Bu | *L*-Leu | 55 | 14 |
| *s*-Bu | *L*-Ile | 63 | 38 |
| Ph | *D*-Phg | 85 | 30 |
| Bn | *L*-Phe | 72 | 28 |
| $CH_2CO_2Me$ | *L*-Asp | 64 | 14 |
| $C_2H_4CO_2Me$ | *L*-Glu | 62 | 28 |

A highly regioselective alkylation of *N*-methyltrimellitic acid imide (**100**) has been recently described.[59] Photolysis in the presence of potassium propionate solely gave the *para*-addition product (**101**) in 84% yield (Scheme 49). Its preferred formation was explained on basis of the differences in spin densities in the corresponding imide radical anions. For the radical anion of **100**, the spin densities were significantly higher for the imido *para*-carbon atom than for the *meta*-carbon atom thus indicating preferential *para* coupling. In contrast, *N*-methylquinolinic acid imide only showed a slight preference for formation of its *ortho* isomer.



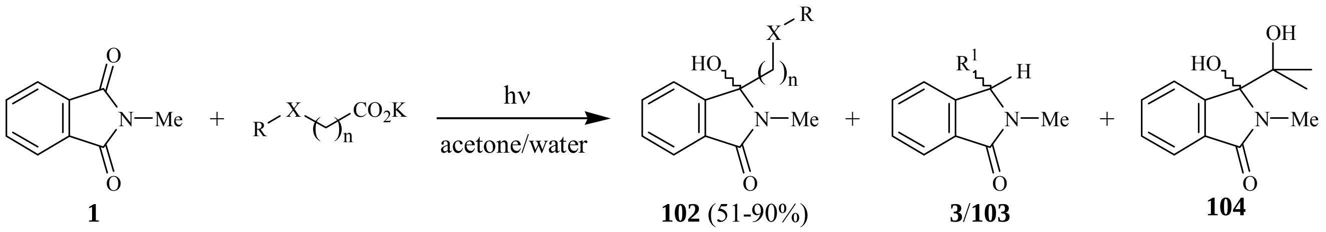
**100** **101** (84%)

Scheme 49

Recently, Griesbeck and coworkers used the photodecarboxylative benzylation of phthalimides as a concise route to *Artistolactam* precursors.[60] However, the necessary final electrocyclization step appears problematic.[61]

## 8.2 Photoadditions of heteroatom substituted carboxylates

The incorporation of additional heteroatoms in the alkylcarboxylate altered the respective electron donor capacity,[62] and either strongly increased or decreased the addition efficiency.[63] α-Thioalkyl- and α-oxoalkyl-substituted carboxylates readily gave the corresponding addition products (**102**) in moderate to good yields of 57-90% from *N*-methylphthalimide (**1**). In sharp contrast, the β-thioalkyl-substituted carboxylate remained inert, whereas the corresponding β- to ω-oxoalkyl carboxylate reacted efficiently to give the addition products in 45-76% yield (Scheme 50; Table 10).[63] Accounting for the different reactivity of sulfur- *vs*. oxygen-substituted carboxylates, it was concluded that oxidation of the heteroatom plays the dominant role for thioethers. In case of the β-thioalkyl substrate, the sulfur atom acts as a hole trap due to fast non-productive back electron transfer[64] and prevents oxidation of the carboxylate. The photoreactions involving alkylamino-substituted carboxylates gave exclusively photoreduction to **103** (**R$^1$** = H) or trapping of the solvent acetone (→ **104**).[63a]



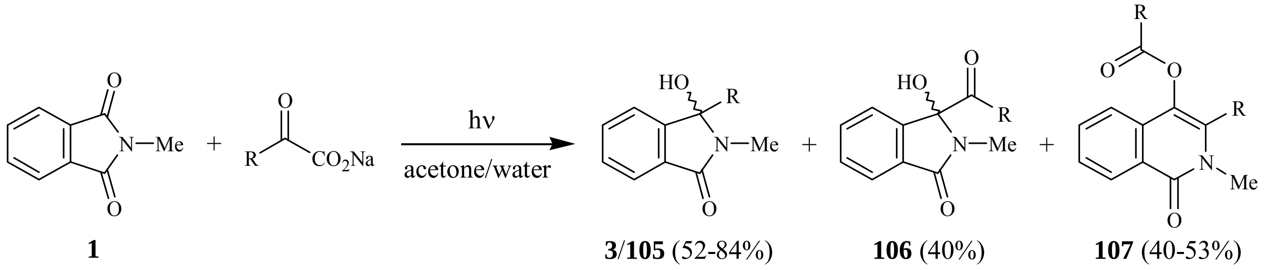
**Scheme 50**

**Table 10** Photoadditions of heteroatom substituted carboxylates to *N*-methylphthalimide (**1**).

| Carboxylate | | | Yields | | |
|---|---|---|---|---|---|
| **X** | n | **R** | **102** [%] | **3/103** [%] | **104** [%] |
| S | 1 | Me | 90 | — | — |
| S | 1 | Ph | 57 | — | — |
| S | 2 | Me | — | — | — |
| O | 1 | Me | 57 | — | — |
| O | 1 | Ph | 73 | — | — |
| O | 1 | 2,4-$Cl_2C_6H_3$ | 76 | — | — |
| O | 2 | Me | 51 | — | — |
| O | 2 | Ph | 65 | — | — |
| O | 3 | Ph | 55 | — | — |
| O | 4 | Ph | 45 | — | — |
| O | 9 | Ph | 47 | — | — |
| O | 10 | Ph | 49 | — | — |
| O | 1 | H | 57 | <5 (**3**: OH) | — |
| NMe | 1 | Me | — | 21 (**103**: H) | — |
| NMe | 2 | Me | — | 57 (**103**: H) | 36 |

### 8.3 Photoadditions of α-keto carboxylates

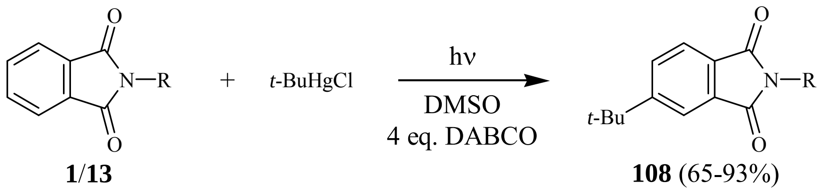
The product spectra from irradiation of phthalimides in the presence of α-keto carboxylates included alkylation, acylation and ring expansion (Scheme 51), respectively.[65] Glyoxylate as well as secondary and tertiary α-keto carboxylates gave the corresponding reduction or alkylation products (**3** and **105**) in yields of 52-86%. On the contrary, pyruvate and α-keto leucine gave dihydroisoquinolinyl esters (**107**) as ring expansion products in yields of 40-53%. In the latter case the acylated product (**106**) was additionally isolated in 43% yield. Based on the results it was assumed that the course of the reaction is controlled by the stability of the acyl radical intermediates.[66] When less reactive acyl radicals are generated, C-C bond formation successfully competes with decarbonylation, whereas in cases of more reactive acyl radicals, decarbonylation preceded C-C-bond formation. The unusual ring-expansion products (**107**) most reasonably originate from the monoacylated compounds (**106**) *via* rearrangement to the corresponding isomeric isoquinolines.



**Scheme 51**

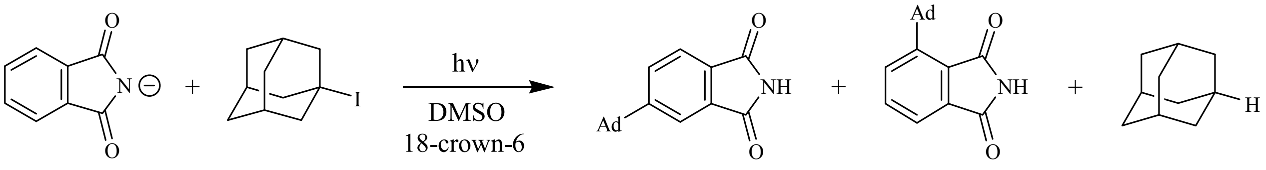
## 9 MISCELLANEOUS REACTIONS

A base-promoted *tert*-butylation at the aromatic core of either *N*-methylphthalimide (**1**) or phthalimide (**13**) involving a thermal electron transfer step was developed by Russell and coworkers.[67] This radical chain reaction is initiated by photochemical cleavage of alkylmercury halides leading to *tert*-butyl radicals which add to the aromatic ring in a highly regioselective fashion (Scheme 52). The yields of the corresponding alkylated phthalimides (**108**) were generally high with 65-93%.



**Scheme 52**

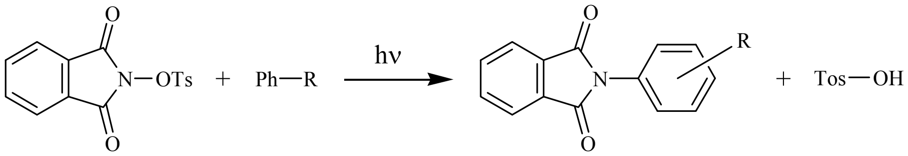
A similar reaction has been described by Peñéñory *et al.* for 1-iodoadamantane and the phthalimide anion (**4**).[68] In this case, however, the regioselectivity decreased and a mixture of **109** and **110** was obtained (Scheme 53). Additionally, a larger amounts of adamantane (**96**) was isolated. The lack of reaction in the dark and inhibition by *p*-nitrobenzene (as radical anion trap), 1,4-cyclohexadiene, and di-*tert*-butyl nitroxide (as radical traps) supported a reaction *via* a $S_{RN}1$ mechanism.



**4** **109** (45%) **110** (12%) **96** (21%)

Scheme 53

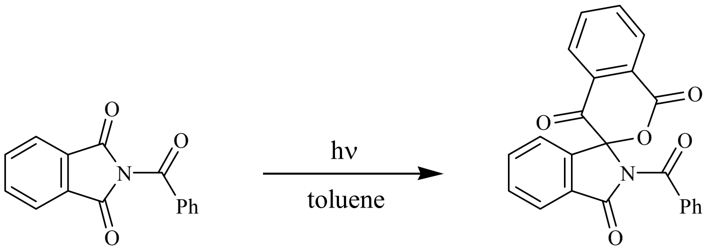
In 1975, Codogan and Rowley described a radical phthalimidation of aromatic compounds using *N*-tosyloxyphthalimide (**111**).[69] Irradiation in the aromatic solvent gave *N*-arylphthalimides (**112**) in moderate to quantitative yields as mixtures of all three isomers (Scheme 54), along with *p*-toluenesulfonic acid. When toluene was used, biphenyl was additionally isolated in 29%, thus indicating a radical mechanism.



**111** **112** (12-100%)

Scheme 54

Recently, Howie *et al.* have reported on the formation of a *spiro*-benzoyltrione compound (**113**) in 50% yield based on a conversion of 17%, from *N*-benzoylphthalimide (**66**) irradiated in toluene (Scheme 55). The compound was thought to be formed from initial photopinacolization, followed by thermal ring opening and subsequent lactonization involving the displacement of benzamide.[70]



**66** **113** (50%)

Scheme 55

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