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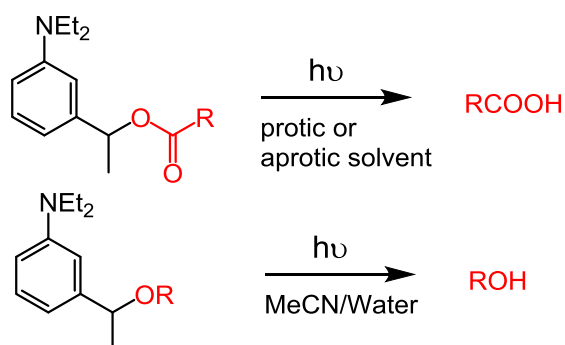
1-[3-(Diethylamino)phenyl]ethyl (DEAPE): A Photolabile Protecting Group for Hydroxyl and Carboxyl Groups

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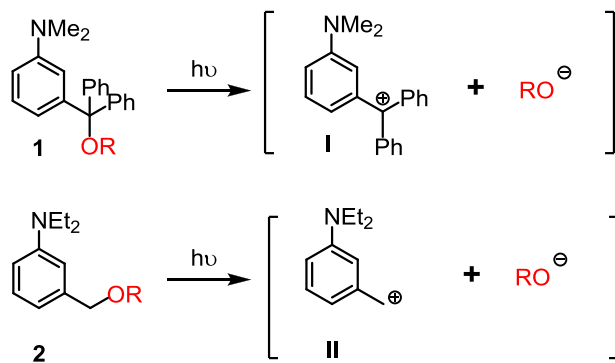
ABSTRACT

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3 Herein we demonstrate that the photolabile protecting group (PPG), 1-[3-(diethylamino)-
4 phenyl]ethyl (DEAPE) group, has dramatically different photochemical properties from the
5 parent 3-(diethylamino)benzyl (DEABn) PPG. The new PPG, derived from DEABn by adding a
6 methyl group to the benzylic carbon, has similar reactivity as DEABn in releasing alcohol in
7 MeCN/water; however, it is more efficient than DEABn in releasing carboxylic acid. In
8 particular, it can release carboxylic acid efficiently in aprotic solvents and the PPG itself
9 converts to 3-diethylaminostyrene. Photochemical removal of DEAPE can also be conveniently
10 carried out with sunlight. The results in this work suggest that there probably exist multiple
11 reaction pathways in cleaving the benzylic C-O bond and they can be affected by the benzylic
12 substitution and the reaction conditions.
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Introduction

Photolabile protecting groups (PPGs) have demonstrated increasingly important role in a broad range of research areas. Some of their creative applications in synthesis,¹ traceless release of biologically important molecules,²⁻⁵ polymers,⁶⁻⁷ and surface patterning⁸⁻⁹ were reviewed recently. Despite the significant advance in the field, there is still demanding for new PPGs to complement the existing arsenal.¹⁰⁻¹¹ We have recently developed a series of structurally simple PPGs for carbonyl, hydroxyl, diol, amino, and carboxyl groups.¹¹⁻¹² For example, the trityl-type hydroxyl PPG, *e.g.*, α,α -diphenyl-3-(diethylamino)benzyl PPG (as in **1**)¹³⁻¹⁴ and the benzyl-type hydroxyl PPG, *e.g.*, 3-diethylaminobenzyl (DEABn) group (as in **2**),¹⁵ are both effective and structurally simple PPGs for releasing hydroxyl groups upon UV irradiation (Scheme 1). These two PPGs have similar chemical and photochemical efficiency in releasing substrates, even though the presumed tritylium intermediate (**I**) of **1** would be much stable than the benzylic cation intermediate (**II**) of **2**. We also noticed that the DEABn PPG released alcohol more efficiently than released carboxylic acid, albeit that carboxylate is a better leaving group. Herein we report that a slight structural variation of the DEABn group can result in a new PPG that not only has improved efficiency in releasing carboxylic acid in protic solvent but also can release the substrate effectively in aprotic solvent, which should further expand application scope of the PPG. Results from this work also provide new insights into the reaction mechanism.

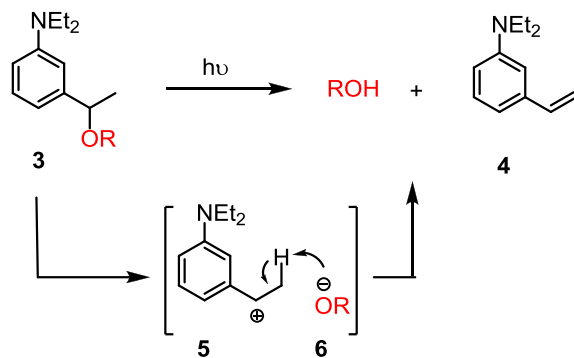
Scheme 1. Trityl-Type and Benzyl-Type PPGs



19 Results and Discussion

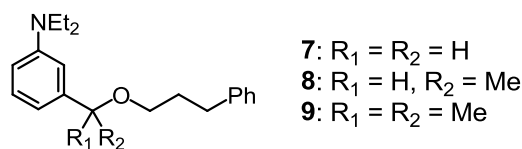
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21 The new PPG, 1-[3-(diethylamino)phenyl]ethyl (DEAPE) PPG as shown in **3** (Scheme 2), is
22 derived from DEABn by adding a methyl group to the benzylic carbon. We inferred that UV
23 irradiation of ether **3** would lead to the ion pair of benzylic cation **5** and alkoxide/carboxylate **6**,
24 and subsequent proton abstraction by **6** from **5** would provide alcohol/carboxylic acid ROH and
25 styrene product **4**. Since benzylic cation **5** can be the proton source for released alkoxide
26 /carboxylate **6**, we reasoned that the reaction could probably take place in aprotic solvent.
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39 Scheme 2. Design of a New Benzyl-Type PPG



We thus compared three benzyl-type PPGs as in **7-9** (Table 1). The un-substituted DEABn PPG in **7** serves as a control, and compound **8** has the DEAPE PPG and compound **9** has the 2-[3-(diethylamino)phenyl]-2-propyl (DEAPP) PPG. Even though the benzylic carbon of the DEAPP PPG is a tertiary carbon center, compound **9** is thermally stable. It remained intact in MeCN/water (4:1) at 50 °C for 2 hours at pH = 7 or 2.

Table 1. Comparison of Bn-Type PPGs in Releasing Alcohol in MeCN/water^a



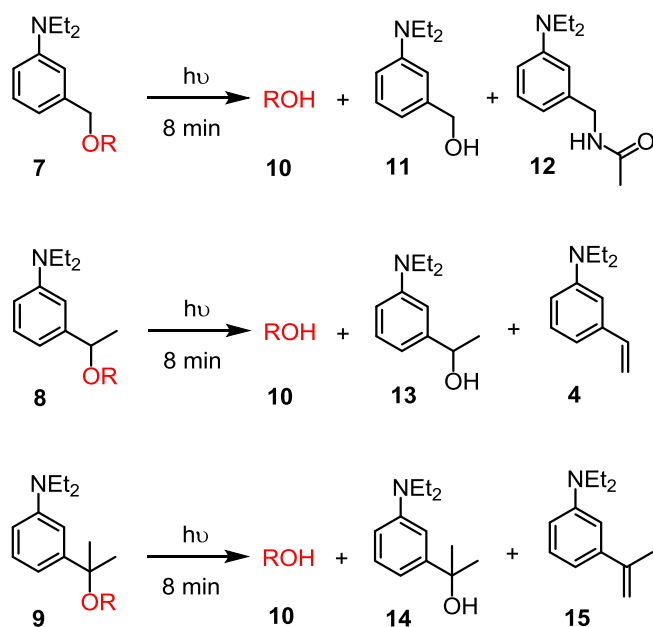
Entry	caged substrate	rxn. time (min)	conv. (%)	released substrate (%)	PPG-OH (amide) (%)	Styrene (%)
1	7	5	76	98	58 (28)	-
2	7	8	94	98	53 (34)	-
3	8	5	75	>99	79	3
4	8	8	96	99	61	2
5	9	5	84	96	80	12
6	9	8	96	99	74	12

^aA 5.0 mM solution in CD₃CN/D₂O (4:1) in 5 mm NMR tubes was irradiated with a 450 W medium pressure mercury lamp equipped with a Pyrex filter sleeve ($\lambda > 300$ nm) without deaeration. The yields were determined by ¹H NMR analysis and calculated based on the corresponding conversion.

We first compared the photoreactions of **7-9** in MeCN in the presence of protic solvent water (Scheme 3). These PPGs showed similar chemical efficiency in MeCN/water (4:1) (Table 1, entries 1-6). For compound **7**, irradiation for 8 min led to release of the alcohol (**10**) in 98% yield (based on 94% conversion) (Table 1, entry 2). The PPG mainly converted to the corresponding

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3 PPG-OH (*i.e.*, 3-diethylaminobenzyl alcohol (**11**)) in 53% yield and *N*-(3-diethylamino)benzyl
4 acetamide (**12**) in 34% yield. The latter was derived from trapping of the benzylic cation with
5 acetonitrile followed by hydrolysis of the resulting nitrilium ion.¹⁵ Compounds **8** and **9** also
6 released the alcohol efficiently; however, their PPGs mainly converted to the respective PPG-
7 OH, *e.g.*, **13** (61%) from **8** (Table 1, entry 4) and **14** (74%) from **9** (Table 1, entry 6) after 8 min
8 of irradiation. The PPG-OHs were unstable under the irradiation conditions. In the case of **8** the
9 yield of **13** decreased from 79% after 5 min of irradiation to 61% after 8 min. We did not observe
10 the respective amide in the reaction mixture of **8** and **9**. The expected styrene products from the
11 corresponding PPG of **8** and **9** were only produced in a minor amount, *e.g.*, 2~3% of **4** from **8**
12 and 12% of **15** from **9** (Table 1, entries 3-6).
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27 **Scheme 3.** Photoreaction of **7-9** in MeCN/water

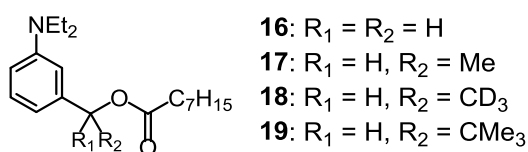


We then examined photoreactions of **7** and **8** in MeCN or DMF without a protic co-solvent. Contrary to what we expected, conversion of **7** and **8** was low in both solvents. For example,

conversion of **8** was only 7% in MeCN and 9% in DMF after 10 min of irradiation. These results suggest that protic solvent such as water is crucial to the photoreactions; it stabilizes the charge-separation transition state and species developed along the reaction pathway of benzylic C-O bond heterolysis through effective solvation. Formation of the PPG-OH and the respective styrene from **8** and **9** in the presence of water indicates possible involvement of competing S_N1 and E1 pathways. Less styrene formation from **8** than from **9** can probably be attributed to an additional S_N2 pathway being available for **8** with its leaving group on the secondary carbon.

Contrary to their similar reactivity in releasing alcohol, DEABn and DEAPE displayed different behaviors in releasing carboxylic acid. We showed previously that DEABn was less efficient in releasing alcohol than releasing acid in MeCN/water, albeit carboxylate is a much better leaving group than alkoxide.¹⁵ With DEABn, ester **16** showed different reactivity in CD₃CN/D₂O (4:1) ($\epsilon_{313 \text{ nm (MeCN/H}_2\text{O)}} = 2,200 \text{ M}^{-1} \text{ cm}^{-1}$) and in CD₃CN ($\epsilon_{308 \text{ nm (MeCN)}} = 2,300 \text{ M}^{-1} \text{ cm}^{-1}$). In CD₃CN/D₂O (4:1), 15 min of irradiation released the acid in 82% yield (based on 70% conversion) (Table 2, entry 1), which was less efficient than that of the ether counterpart under the same reaction conditions (Table 1, entries 1 and 2). These results are consistent with our earlier observations.¹⁵ In CD₃CN without protic co-solvent, photoreaction of **16** released the acid in 62% yield (based on only 33% conversion) under the same conditions (Table 2, entry 2), much less efficient and clean than the reaction in CD₃CN/D₂O (4:1).

Table 2. Comparison of Bn-Type PPGs in Releasing Carboxylic Acids^a



Entry	caged substrate	solvent	rxn Time (min)	conv. (%)	released substrate (%)	PPG-OH (amide) (%)	Styrene 4 (%)
1	16	CD ₃ CN/D ₂ O 4:1	15	70	82	41 (24)	-
2	16	CD ₃ CN	15	33	62	-	-
3	17	CD ₃ CN/D ₂ O 4:1	10	85	96	28	47
4	17	CD ₃ CN/D ₂ O 4:1	15	95	94	30	36
5	17	CD ₃ CN	10	83	92	-	61
6	17	CD ₃ CN	15	88	96	-	53
7	17	CH ₃ CN	15	89	95(91 ^b)	-	40 (40 ^b)
8	17	CD ₃ CN (N ₂)	20	87	96	-	75
9	18	CD ₃ CN	15	82	98	-	-
10	19	CD ₃ CN	15	90	18	-	-
11	19	CD ₃ CN/D ₂ O 4:1	15	94	84	-	-

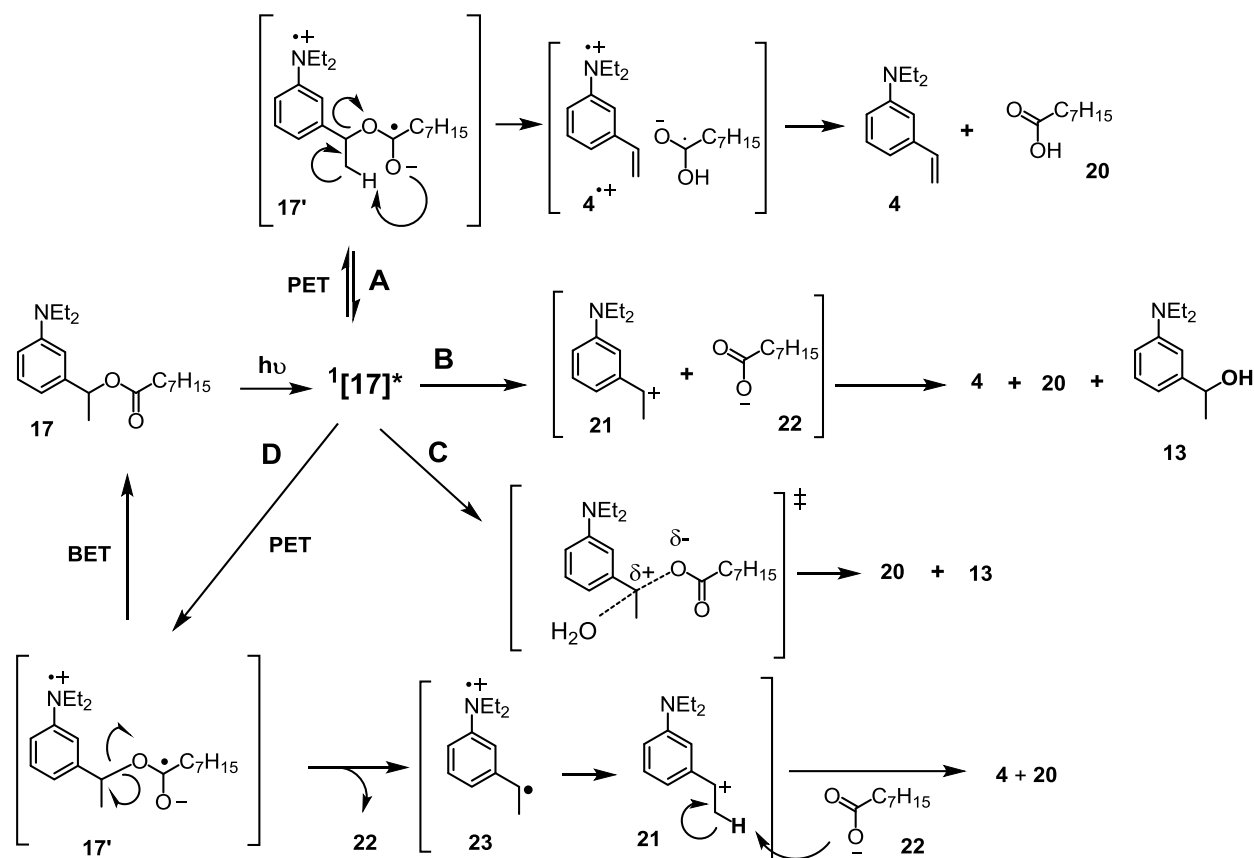
^aA 5.0 mM solution in CD₃CN/D₂O (4:1) in 5 mm NMR tubes was irradiated with a 450 W medium pressure mercury lamp equipped with a Pyrex filter sleeve ($\lambda > 300$ nm) without deaeration. The yields were determined by ¹H NMR analysis and calculated based on the corresponding conversion. ^bIsolated yield.

However, DEAPE showed much improved efficiency in releasing acid compared with DEABn. For instance, ester **17** in CD₃CN/D₂O (4:1) ($\epsilon_{314 \text{ nm (MeCN/H}_2\text{O)}} = 2,400 \text{ M}^{-1} \text{ cm}^{-1}$, $\phi = 0.16$) released the acid in 96% yield (based on 85% conversion) after only 10 min of irradiation, and in 94% yield (based on 95% conversion) after 15 min irradiation. The PPG converted to the PPG-OH and the expected styrene, *i.e.*, compound **4** (Table 2, entries 3 and 4). Contrary to DEABn, photoreaction of **17** ($\epsilon_{308 \text{ nm (MeCN)}} = 2,500 \text{ M}^{-1} \text{ cm}^{-1}$, $\phi = 0.15$) was equally efficient in MeCN in the absence of water. For example, release of the acid was in 92% yield (based on 83% conversion) after 10 min of irradiation and in 95% yield (based on 88% conversion) after 15 min of irradiation in MeCN (Table 2, entries 5-8). PPG product **4** was in 61% yield at 10 min and decreased to 53% yield at 15 min; however, it was in 75% yield at 20 min if the reaction was under nitrogen atmosphere (Table 2, entry 8). It appeared that the

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3 presence of oxygen would not affect release of the carboxylic acid but accelerate decomposition
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5 of styrene **4** under irradiation. In a larger scale run of the reaction in CH₃CN, the reaction
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7 outcome (Table 2, entry 7) was close to the small scale run in CD₃CN (Table 2, entry 6). The
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9 released acid was isolated in 91% yield (based on 89% conversion), in agreement with the
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11 calculated yields based on ¹H NMR analysis.
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15 DEAPE showed much better efficiency in releasing acid than releasing alcohol in MeCN,
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17 different from its reactivity shown in MeCN/water solution. For example, in MeCN, conversion
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19 of ether **8** after 10 min irradiation was only 7% (versus 83% conversion of **17**). These
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21 experimental observations suggest that the ester group perhaps played a role in facilitating the
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23 benzylic C-O bond scission. We first postulated a possible pathway that involved a photo-
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25 induced single electron transfer process (PET) upon irradiation of **17** (*i.e.*, pathway A, Scheme
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27 4).¹⁶⁻²⁰ The resulting ionic diradical intermediate **17'** would undergo intramolecular proton
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29 abstraction to provide the radical cation of **4** and the corresponding radical anion of the released
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31 acid. Subsequent SET within the pair would result in styrene **4** and carboxylic acid **20**.
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40 **Scheme 4.** Proposed Reaction Mechanism of Photo Deprotection
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To test this hypothesis, we examined photoreaction of **18** that possesses a α CD₃ group instead of a CH₃ group as in **17**. After irradiation for 6 min under the same reaction conditions, conversion of **17** and **18** were 57% and 56%, respectively, and after irradiation for 15 min, conversion of **17** and **18** were 88% and 82%, respectively (Table 2, entry 6 vs. 9). The small hydrogen isotope effect (even for a non-linear hydrogen transfer), suggests that fragmentation of **17'** was probably not starting with proton abstraction from the benzylic α methyl group by the radical anion of the ester moiety or via a concerted process, thus pathway A might not operate. The photoreaction of **19** with a α *tert*-butyl group did not provide further mechanistic insights. Irradiation of **19** in CD₃CN resulted in a complex mixture containing multiple products derived

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3 from the carboxylic acid part with the desired acid in only 18% yield (based on 90% conversion)
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5 (Table 2, entry 10). However, in CD₃CN/D₂O (4:1), the carboxylic acid was released in 84%
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7 yield (based on 94% conversion) (Table 2, entry 11) while the PPG portion converted to a
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9 complex mixture.
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13 Based on the experimental observations, we proposed other possible pathways for the
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15 photoreaction of **17** (Scheme 4). Thus in pathway B, direct benzylic C-O cleavage can take place
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17 in the S₁ state of **17**, leading to benzylic cation **21** and carboxylate **22**. In the presence of a protic
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19 solvent, *e.g.*, in MeCN/water solution, the competing S_N1 and E1 mechanisms would lead to
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21 solvolysis product **13** and elimination product **4**, respectively, from benzylic cation **21**, along
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23 with released carboxylic acid **20** (Table 2, entries 3 and 4). The similar pathway is probably also
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25 involved in releasing alkoxide in **7-9**. However, for a poor leaving group like alkoxide, solvation
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27 of the leaving group in the transition state by protic solvent molecules would be crucial to bond
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29 cleavage. Alternatively, a S_N2-like mechanism (*i.e.*, pathway C) would release acid **20** and
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31 produce solvolysis product **13** without producing styrene **4**. Pathway C should be more important
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33 for releasing poor leaving group alkoxide than releasing carboxylate. In fact, in the reaction of
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35 ether **8**, there were much more PPG-OH **13** than styrene **4** (*e.g.*, 79% *vs.* 3%, Table 1, entry 3)
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37 while in the reaction of ester **17**, there were less solvolysis product **13** than styrene **4** (*e.g.*, 28%
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39 *vs.* 47%, Table 2, entry 3). Another reason for the higher production of elimination than
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41 solvolysis could be the involvement of pathway D in the photolysis of **17** (Scheme 4). Thus,
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43 intermediate **17'** can undergo homolysis of the benzylic C-O bond to release carboxylate **22** and
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45 produce cationic diradical intermediate **23**.¹⁶⁻²⁰ This open-shell diradical intermediate might
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47 convert to closed-shell benzylic cation **21**, since it was estimated that the triplet of intermediate
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49 **23** was ~11.2 kcal/mol higher of energy than ground state benzylic cation **21** based on density
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3 functional theory (DFT) computation (B3LYP/6-31G(d,p)).²¹ Intermediate **21** would lead to
4 styrene **4** as in pathway B. Pathways **B-D** would all contribute to the overall efficiency of
5 photochemical release of carboxylic acid **20** in the presence of protic solvent but only pathway D
6 would operate in aprotic solvent. We inferred that pathway D might be available for DEABn as
7 well. However, DEABn released carboxylate in lower efficiency than that of DEAPE (Table 2,
8 entries 2 and 6), and this difference in reactivity can be attributed to the fact that the secondary
9 benzylic radical intermediate of DEAPE (*i.e.*, **23**) is more stable than the primary benzylic
10 radical of the DEABn counterpart. For the same reason, the competing non-productive back
11 electron transfer (BET) process probably did not affect **17** (*i.e.*, from **17'** to **17** in pathway D) as
12 much as affect **16**. We attributed the BET process of DEABn for its lower efficiency in releasing
13 carboxylate than releasing alkoxide.¹⁵
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29 DEAPE released carboxylic acid not only in aprotic solvent MeCN but also in some other
30 aprotic solvents such as DMSO, DMF, or acetone. For example, irradiation of **17** in DMF-d7 led
31 to higher conversion and better yield of the styrene product from the PPG than in CD₃CN (Table
32 3, entries 1-4). Again, styrene was not stable under the irradiation conditions, and its yield
33 decreased with increased time of UV exposure. Under nitrogen atmosphere in DMF, the yield of
34 the released acid improved slightly but styrene **4** appeared to be more stable (Table 3, entry 5).
35 Similar results were obtained in DMSO (Table 3, entries 6 and 7) and acetone (Table 3, entries 8
36 and 9), but in acetone, styrene **4** was much less stable, and the signals of the PPG in the aromatic
37 region of the ¹H NMR became very complicated. Photochemical reactions of **17** to release the
38 acid also occurred in EtOAc, hexanes, benzene, and THF but the results were not better than
39 those shown in Table 2 and 3.
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Table 3. Irradiation of **17** in different aprotic solvents ^a

Entry	solvent	rxn Time (min)	conv. (%)	released substrate (%)	Styrene 4 (%)
1	CD ₃ CN	10	83	92	61
2	CD ₃ CN	15	88	96	53
3	DMF	10	94	90	76
4	DMF	15	100	87	66
5	DMF	30 ^b	100	94	74
6	DMSO	10	87	92	70
7	DMSO	15	95	91	39
8	Acetone	10	89	86	13
9	Acetone	15	95	88	9

^aA 5.0 mM solution in deuterated solvent in a 5 mm NMR tube was irradiated with a 450 W medium pressure mercury lamp equipped with a Pyrex filter sleeve ($\lambda > 300$ nm) without deaeration. The yields were determined by ¹H NMR analysis and calculated based on the corresponding conversion. ^bUnder N₂

The new PPGs can also release alcohol and acid with sunlight. For example, irradiation of **9** in CD₃CN/D₂O (4:1) for 30 min under sunlight (with a local UV index of 6) released the alcohol in 98% yield (based on 83% conversion). The PPG converted to the corresponding PPG-OH (84%) and styrene (8%) (Table 4, entry 1). The photoreaction completed in 60 min with a nearly quantitative yield of the released alcohol (Table 4, entry 2). Reaction of **17** in CD₃CN under sunlight (with a local UV index of 5) also released the acid in excellent yields (Table 4, entries 3-6). The yield of the PPG product, *i.e.*, styrene **4**, diminished with increased time of sunlight exposure, which is consistent with the observations made with the reactions carried out with the UV lamp.

Table 4. Photoreaction with sunlight^a

Entry	caged substrate	solvent	rxn Time (min)	conv. (%)	released substrate (%)	PPG-OH (%)	Styrene (%)
1	9	CD ₃ CN/D ₂ O 4:1	30	83	98	84	8
2	9	CD ₃ CN/D ₂ O 4:1	60	100	>99	ND	ND
3	17	CD ₃ CN	30	30	95	-	66
4	17	CD ₃ CN	60	54	91	-	67
5	17	CD ₃ CN	120	77	87	-	49
6	17	CD ₃ CN	210	88	88	-	39

^aA 5.0 mM solution in deuterated solvent in a 5 mm NMR tube was irradiated with sunlight without deaeration. The yields were determined by ¹H NMR analysis and calculated based on the corresponding conversion.

Conclusion

In conclusion, we demonstrated that with slight structural variation from DEABn, the resulting DEAPE PPG showed dramatically different photochemical properties from the parent DEABn PPG. It is not only more efficient than DEABn in releasing carboxylic acid but also can release carboxylic acid efficiently in aprotic solvent such as MeCN, DMF, DMSO, and acetone. In the photoreaction of releasing carboxylic acid, the DEAPE PPG mainly converted to 3-diethylamino styrene. Comparison of the reaction results of DEAPE in releasing alcohol and acid under different conditions provided mechanistic insights, revealing that there could be multiple reaction pathways involved in photochemical cleavage of the benzylic C-O bond. In releasing alcohol from DEABn (as in **7**) and DEAPE (as in **8**), we postulated that the reaction was mainly taking place via a UV-triggered S_N2 pathway with the protic solvent serving as the nucleophile. There also existed a S_N1 pathway for DEAPP (as in **9**), as evidenced by the presence of a small amount of styrene in the reaction products. In releasing carboxylic acid from DEAPE, in addition

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3 to the S_N2 and S_N1 pathways in protic solvent, there could be a PET-promoted pathway leading
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5 to homolysis of the benzylic C-O bond. The resulting cationic diradical intermediate would
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7 convert to the ground-state benzylic cation, which justified the high productivity of styrene from
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9 the PPG in the process or releasing acid and the high efficiency of the photoreaction in aprotic
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11 solvent where the S_N2 and S_N1 pathways are absent.
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Experimental Section

General. Organic solutions were concentrated by rotary evaporation at ca. 12 Torr. Flash column chromatography was performed employing 230-400 mesh silica gel. Thin-layer chromatography was performed using glass plates pre-coated to a depth of 0.25 mm with 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). IR data are presented as frequency of absorption (cm^{-1}). ^1H NMR or ^{13}C NMR spectra were recorded on 400 and 700 MHz NMR spectrometers; chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CHCl_3 : δ 7.26). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet and/or multiple resonances), coupling constant in Hertz (Hz), integration. HRMS was conducted with ESI ionization method and with TOF mass analyzer.

Materials. Anhydrous solvents diethyl ether (Et_2O), tetrahydrofuran (THF), dimethylformamide (DMF), and dichloromethane (DCM) were used without distillation. Solvents for workup and column chromatography such as petroleum ether (PE), hexanes (Hex), and ethyl acetate (EA), and other chemicals were obtained from commercial vendors and used without further purification.

Synthesis of 1-[3-(diethylamino)phenyl]ethyl 3-phenylpropyl ether (**8**): To the solution of 3-(diethylamino)benzaldehyde (1.80 g, 10.0 mmol) in Et_2O (6.0 mL) was added CH_3MgBr (3.0 M in Et_2O , 3.0 mL, 18.0 mmol) at room temperature and stirred for 2 h. The reaction was then quenched with 1.0 N HCl at 0 °C, extracted with EA, concentrated, and purified by flash column chromatograph (Hex/EA 30:1) to provide 1-[3-(diethylamino)phenyl]ethanol (1.78 g, 92%) as a

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3 colorless oil. Rf = 0.1 (Hex/EA 30:1). To the PPG-OH (96.5 mg, 0.5 mmol) in DMF (3.0 mL)
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5 was added NaH (60%, 60.0 mg, 1.5 mmol) at room temperature, followed by 3-phenylpropyl
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7 tosylate (218.0 mg, 0.75 mmol). The reaction completed in 24 h and was then quenched with ice
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9 water, extracted with EA. The organic layer was washed with water, dried over Na₂SO₄,
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11 concentrated, and purified with flash column chromatography (Hex/EA 100:1) to provide **8**
12
13 (139.0 mg, 89%) as a colorless oil. Rf = 0.10 (Hex/EA 100:1); ¹H NMR (700 MHz, CDCl₃) δ
14
15 7.27-7.23 (m, 2 H), 7.18-7.14 (m, 4 H), 6.66 (s, 1 H), 6.60-6.56 (m, 2 H), 4.31 (q, *J* = 6.5 Hz, 1
16
17 H), 3.42-3.30 (m, 6 H), 2.74-2.62 (m, 2 H), 1.90 (quint, *J* = 7.4 Hz, 2 H), 1.44 (d, *J* = 6.5 Hz, 3
18
19 H), 1.16 (t, *J* = 7.1 Hz, 6 H); ¹³C NMR (176 MHz, CDCl₃) δ 148.0, 145.2, 142.3, 129.2, 128.5,
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21 128.3, 125.7, 113.5, 110.8, 109.2, 78.5, 67.9, 44.4, 32.5, 31.6, 24.3, 12.6; IR (neat) 3027, 2970,
22
23 2929, 2864, 1600, 1495, 1448; HRMS (ESI-TOF) *m/e*: calc for C₂₁H₃₀NO [M+H]⁺ 312.2327,
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25 found 312.2334.
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33 Synthesis of 2-[3-(diethylamino)phenyl]-2-propyl 3-phenylpropyl ether (**9**): Compound **9**
34
35 was obtained in a way similar to that described for **8** and the reaction of 2-[3-(diethylamino)-
36
37 phenyl]-2-propanol with 3-phenylpropyl tosylate provided **9** in 76% yield. Rf = 0.2 Hex/EA
38
39 50:1); ¹H NMR (700 MHz, CDCl₃) δ 7.26-7.24 (m, 2 H), 7.18-7.15 (m, 4 H), 6.81 (s, 1 H), 6.64
40
41 (d, *J* = 7.6 Hz, 1 H), 6.59 (d, *J* = 8.2 Hz, 1 H), 3.36 (q, *J* = 7.0 Hz, 4 H), 3.24 (t, *J* = 6.6 Hz, 2
42
43 H), 2.66 (t, *J* = 7.9 Hz, 2H), 1.87 (quint, *J* = 7.9 Hz, 2 H), 1.53 (s, 6 H), 1.16 (t, *J* = 7.0 Hz, 6 H);
44
45 ¹³C NMR (176 MHz, CDCl₃) δ 147.8, 147.6, 142.4, 128.9, 128.4, 128.2, 125.6, 113.2, 110.5,
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47 109.4, 62.1, 44.4, 32.6, 32.2, 28.6, 12.7; IR (neat) 3026, 2972, 2929, 2867, 1598, 1576, 1493;
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49 HRMS (ESI-TOF) *m/e*: calc for C₂₂H₃₂NO [M+H]⁺ 326.2484, found 326.2483.
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3 Synthesis of 1-[3-(diethylamino)phenyl]ethyl octanoate (**17**): To the solution of 1-[3-
4 (diethylamino)phenyl]ethanol (309.0 mg, 1.60 mmol) in DCM (4.0 mL) at room temperature was
5 added octanoyl chloride (274.0 mg, 1.68 mmol) and DMAP (2.0 mg). The reaction completed
6 after stirring overnight and was quenched with ice water. The DCM layer was washed with
7 water, brine, dried over anhydrous Na₂SO₄, and concentrated. The residue was purified with
8 flash column chromatography ((PE/EA) to provide **17** (488.0 mg, 95%) as a colorless oil. R_f =
9 0.2 (PE/EA 50:1); ¹H NMR (700 MHz, CDCl₃) δ 7.17 (t, *J* = 8.1 Hz, 1 H), 6.64-6.59 (m, 3 H),
10 5.83 (q, *J* = 6.6 Hz, 1 H), 3.35 (q, *J* = 7.1 Hz, 4 H), 2.31 (m, 2 H), 1.63 (quint, *J* = 7.3 Hz, 2 H),
11 1.52 (d, *J* = 6.6 Hz, 3 H), 1.29-1.26 (m, 8 H), 1.16 (t, *J* = 7.1 Hz, 6 H), 0.87 (t, *J* = 7.1 Hz, 3 H);
12 ¹³C NMR (176 MHz, CDCl₃) δ 173.2, 147.9, 142.8, 129.4, 112.9, 111.2, 109.5, 72.6, 44.4, 34.7,
13 31.7, 29.1, 28.9, 25.0, 22.6, 22.3, 14.1, 12.6; IR (neat) 2963, 2927, 2858, 1732, 1603, 1581,
14 1499; HRMS (ESI-TOF) *m/e*: calc for C₂₀H₃₄NO₂ [M+H]⁺ 320.2590, found 320.2594.
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33 Synthesis of 1-[3-(diethylamino)phenyl]-2,2,2-trideuterioethyl octanoate (**18**): To the
34 mixture of Mg (41.0 mg, 1.7 mmol) in 2.0 mL of Et₂O was added CD₃I (218.0 mg, 1.50 mmol)
35 under N₂. The reaction mixture was initiated at warm temperature and then stirred at room
36 temperature for 2.5 h. The solution of 3-(diethylamino) benzaldehyde (177.0 mg, 1.0 mmol) in
37 1.0 mL of Et₂O was then added and stirred at room temperature for 1.5 h, and the reaction was
38 quenched with ice water and neutralized with 1N HCl. The organic layer was separated, dried
39 over Na₂SO₄, and concentrated. The crude product mixture was purified with flash column
40 chromatography (Hex/EA 5:1, R_f = 0.3) to provide the corresponding PPG-OH (**S1**) (141 mg,
41 72%) as a colorless oil. ¹H NMR (700 MHz, CDCl₃) δ 7.19 (t, *J* = 7.9 Hz, 1 H), 6.70 (s, 1 H),
42 6.64 (dd, *J* = 7.5, 0.5 Hz, 1 H), 6.60 (dd, *J* = 8.3, 2.6 Hz, 1 H), 4.82 (s, 1 H), 3.36 (q, *J* = 7.1, 4
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3 H), 1.16 (t, $J = 7.1$ Hz, 6 H); ^{13}C NMR (176 MHz, CDCl_3) δ 148.1, 147.1, 129.5, 112.3, 111.0,
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5 108.6, 70.9, 44.3, 12.6; IR (neat) 3369, 2969, 2929, 2873, 1600, 1495; HRMS (ESI-TOF) m/e :
6
7 calc for $\text{C}_{12}\text{H}_{17}\text{D}_3\text{NO}$ $[\text{M}+\text{H}]^+$ 197.1733, found 197.1730.
8
9

10 The PPG-OH (49.0 mg, 0.25 mmol), octanoyl chloride (61.0 mg, 0.37 mmol), K_2CO_3
11 (104.0 mg, 0.75 mmol), and DMAP (1 mg) in 2.0 mL of DCM were stirred at room temperature
12 for 4 h. The reaction mixture was filtered to remove the solid and the filtrate was concentrated.
13
14 The crude product mixture was purified with flash column chromatography (Hex/EA 20:1, $R_f =$
15 0.3) to provide ester **18** (75.0 mg, 93%) as a colorless oil; ^1H NMR (700 MHz, CDCl_3) δ 7.17 (t,
16
17 $J = 8.01$ Hz, 1 H), 6.63-6.62 (m, 2 H), 6.60 (d, $J = 7.9$ Hz, 1 H), 5.82 (s, 1 H), 3.35 (q, $J = 7.1$
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19 Hz, 4 H), 2.31 (m, 2 H), 1.63 (quint, $J = 7.1$ Hz, 2 H), 1.29-1.25 (m, 8 H), 1.16 (t, $J = 7.1$ Hz, 6
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21 H), 0.87 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (176 MHz, CDCl_3) δ 173.2, 147.9, 142.8, 129.4, 112.9,
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23 111.2, 109.5, 72.5, 44.4, 34.7, 31.7, 29.1, 28.9, 25.0, 22.6, 14.1, 12.6; IR (neat) 2961, 2927,
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25 2858, 1732, 1603, 1581, 1499; HRMS (ESI-TOF) m/e : calc for $\text{C}_{20}\text{H}_{34}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 320.2590,
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27 found 320.2594.
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36 Synthesis of 1-[3-(diethylamino)phenyl]-2,2-dimethylpropyl octanoate (**19**): To the
37 solution of 3-(diethylamino) benzaldehyde (354.0 mg, 2.0 mmol) in 5.0 mL of THF was added *t*-
38
39 BuMgCl (1.7 M in THF, 1.5 mL, 2.6 mmol) at 0 °C. The reaction mixture was stirred at 50 °C
40
41 for 3 h and quenched with 1.0 N HCl at 0 °C. The aqueous layer was extracted with EA, and the
42
43 organic layer was concentrated, and purified with flash column chromatography (Hex/EA 30:1,
44
45 $R_f = 0.3$) to provide the corresponding PPG-OH (**S2**) (306.0 mg, 65%) as a colorless oil; ^1H
46
47 NMR (700 MHz, CDCl_3) δ 7.14 (t, $J = 7.9$ Hz, 1 H), 6.63 (s, 1 H), 6.60-6.57 (m, 2 H), 4.43 (s,
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49 1 H), 3.35 (m, 4 H), 1.15 (t, $J = 7.1$ Hz, 6 H), 0.95 (s, 9 H); ^{13}C NMR (176 MHz, CDCl_3) δ
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51 147.3, 143.4, 128.4, 115.1, 111.3, 111.0, 83.0, 44.4, 35.6, 26.2, 12.7; IR (neat) 3451, 2968,
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3 2902, 2869, 1600, 1578, 1496; HRMS (ESI-TOF) m/e : calc for $C_{15}H_{26}NO$ $[M+H]^+$ 236.2014,
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5 found 236.2015.
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8 The PPG-OH (47.0 mg, 0.20 mmol), octanoyl chloride (49.0 mg, 0.30mmol), K_2CO_3
9
10 (83.0 mg, 0.60 mmol) in 1.0 mL of DCM were stirred at room temperature overnight. The
11
12 reaction mixture was filtered to remove the solid and the filtrate was concentrated. The crude
13
14 product mixture was purified with flash column chromatography (Hex/EA 20:1, $R_f = 0.4$) to
15
16 provide ester **18** (68.0 mg, 94%) as a colorless oil; 1H NMR (700 MHz, $CDCl_3$) δ 7.11 (t, $J = 8.1$
17
18 Hz, 1 H), 6.58-6.55 (m, 3 H), 5.44 (s, 1 H), 3.37-2.28 (m, 4 H), 2.38-2.31 (m, 2 H), 1.64 (quint, J
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20 = 7.3 Hz, 2 H), 1.29-1.26 (m, 8 H), 1.15 (t, $J = 7.0$ Hz, 6 H), 0.94 (s, 9 H), 0.87 (t, $J = 7.0$ Hz, 3
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22 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.9, 147.1, 139.5, 128.3, 115.3, 111.7, 111.1, 83.0, 44.4,
23
24 35.2, 34.8, 31.7, 29.2, 29.0, 26.3, 25.1, 22.6, 14.1, 12.7; IR (neat) 2960, 2928, 2866, 1735, 1602,
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26 1579, 1499; HRMS (ESI-TOF) m/e : calc for $C_{23}H_{40}NO_2$ $[M+H]^+$ 362.3059, found 362.3044.
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33 Photoreaction of 1-[3-(diethylamino)phenyl]ethyl octanoate (**17**): The solution of **17**
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35 (80.0 mg, 0.25mmol) in 50mL of CH_3CN was allotted to 5 mm NMR tubes (1.5 mL/per tube).
36
37 The samples were irradiated with a 450 W medium pressure mercury lamp in a Hanovia
38
39 photoreactor. With the 450 W medium pressure mercury lamp, the 313 nm UV emission is
40
41 measured to be ~ 1 mW/cm² (at a distance of ~ 4 cm from the UV lamp) with a UVX radiometer.
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43 The radiometer with an attenuator is placed behind a quartz cuvette (1.0 cm) containing a
44
45 solution of 2.0 mM K_2CrO_4 in a 5% K_2CO_3 aqueous solution. After 15 min, the reaction
46
47 solutions were combined and washed with 1.0 N HCl (25 mL) and extracted with ether (30 mL x
48
49 2). The organic layers were combined, dried over anhydrous Na_2SO_4 , and concentrated.
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51
52 Conversion of the reaction was measured to be 89% based on 1H NMR analysis of the crude
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54 product mixture. The crude mixture was purified with flash column chromatography (Hex/EA=
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3 10:1, Rf = 0.1) to provide the acid (29.0 mg, 81%). This yield was 91% based on the 89% of
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5 conversion. The aqueous was concentrated via evaporation and the residue was purified with
6
7 flash column chromatography (Hex/EA 30:1, Rf = 0.5) to provide 3-diethylamino styrene **4** (19.0
8
9 mg, 36%) in its HCl salt form. ¹H NMR (700 MHz, CD₃CN) δ 7.12 (t, *J* = 7.9 Hz, 1 H), 6.73 (s,
10
11 1 H), 6.72-6.67 (m, 2 H), 6.61 (dd, *J* = 8.3, 2.3 Hz, 1 H), 5.73 (dd, *J* = 17.6, 0.9 Hz, 1 H), 5.17
12
13 (d, *J* = 10.9, 0.9 Hz, 1 H), 3.37 (q, *J* = 7.0 Hz, 4 H), 1.12 (t, *J* = 7.0 Hz, 6 H); ¹³C NMR (176
14
15 MHz, CD₃CN) δ 149.2, 139.5, 139.0, 130.4, 114.1, 113.6, 112.7, 110.9, 45.0, 12.9; IR (neat)
16
17 3084, 2967, 2928, 2872, 1731, 1595, 1572, 1495; HRMS (ESI-TOF) *m/e*: calc for C₁₂H₁₈N
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19 [M+H]⁺ 176.1439, found 176.1434.
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25 Photoreaction with sunlight: The 5 mm NMR tubes containing **9** (5.0 mM) in
26
27 CD₃CN/D₂O (4:1) were placed outdoor in sunlight (with a UV index of 5 and temperature of 21
28
29 °C during the reaction time).
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33 Quantum yield determination: A 5.0 mM solution of the sample and a 5.0 mM solution of
34
35 DEABn-protected 3-phenyl-1-propanol (with known quantum yield of 0.26)¹⁵ in NMR tube were
36
37 placed behind a standard 1 cm quartz UV cuvette contain the filter solution. Filtered light
38
39 centered at 312 nm was obtained by passing light from the 450 W medium pressure mercury
40
41 lamp through a solution of 2.0 mM K₂CrO₄ in a 5% K₂CO₃ aqueous solution.²²⁻²³ The yields of
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43 photo reactions were determined by ¹H NMR analysis.
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50 **Supporting Information Available:** ¹H and ¹³C NMR spectra of new compounds, and computation
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52 parameters. This material is available free of charge via the Internet at <http://pubs.acs.org>.
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