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Reaction of Carbenes with Cyclic Ethers in the Presence of Nucleophiles. A Three-Component Coupling Reaction#

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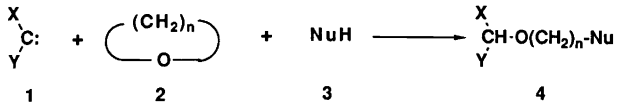
Ternary reaction systems consisting of a carbene [phenylcarbene, ethoxycarbonylcarbene, ethoxy(phenyl)carbene], a cyclic ether (THF, THP) and a protic nucleophile (alcohol, water, carboxylic acid, thiol, or amine) give the corresponding three-component coupling products which are produced via ethereal oxonium ylide intermediates. The mechanism leading to the product formation has been studied in which protonation of carbenes is excluded.

In a variety of ylides formed between carbenes and heteroatoms,[1] the formation of oxonium ylides with ethereal or hydroxy oxygen atoms has been only indirectly proposed. Almost 25 years ago Nozaki's group proposed the intermediacy of a three-membered oxonium ylide in the reaction of styrene oxide with diazoacetate.[2] Later on, a number of cyclic oxonium ylides appeared in the literature: 5-membered ylides were reported by Gilbert for diazoalkene[3] and base-induced reaction of alkenyl triflate with tetrahydrofuran (THF).[4] For oxetane Kirmse and his collaborators carried out systematic studies to prove that a cyclic oxonium ylide is the key intermediate of the reaction.[5] On the other hand, a long-term study with regard to intervening reactive species in the reaction of singlet carbenes with alcohols is continuing, although seems to have been concluded by Kirmse and Kilian for the protonation pathway.[6]

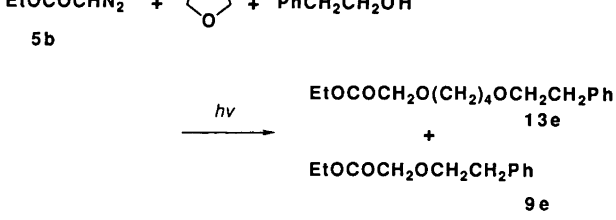
With curiosity not only about the mechanism but also for synthetic utility of ethereal ylides, we chose the reaction of carbenes (**1**) with cyclic ethers (**2**) and nucleophiles (**3**) to realize a synthetic method of introducing two different substituents at both termini of a carbon chain (C_{4-5}), in other words, a method of combining three different components (**1–3**) into one structure (**4**).



1 2 3 4 (1)

Results and discussion

Relative reactivity of THF vs. alcohol in the reaction with ethoxycarbonylcarbene (**1b**). Prior to examining three-component coupling reactions [eqn. (1)], we investigated possible conditions thought to be advantageous to the formation of ethereal ylides between **1** and **2** compared with the protonation of carbenes (**1**) by alcohols (**3**). During the last decade we learnt that, in the reaction with alcohols,[7] carbenes are prone to protonation to produce a carbocation–alkoxide ion pair. Therefore, the relative reactivity of a cyclic ether (THF or THP) vs. an alcohol in the reaction with a carbene (phenylcarbene or alkoxycarbonylcarbene) must be clarified at the beginning of our present study. For this purpose we examined the photolysis reaction of ethyl diazoacetate (**5b**) with a mixture of THF and 2-phenylethanol [eqn. (2)] because we knew that it produces both protonation product (**9e**, O–H insertion product) and three-component coupling product (**13e**), competitively. In the reaction, the molar ratio of THF to phenylethanol was continuously changed from 1 : 9 to 1 : 0.7 while keeping the molar ratio of diazoacetate **5b** to the reactant (alcohol + THF) at a constant 1 : 20. By plotting the molar ratio of products **13e**/(**13e** + **9e**) vs. the ratio of initial concentration of reactants $[THF]_0/([2\text{-phenylethanol}]_0 + [THF]_0)$, the relative reactivity of 2-phenylethanol vs. THF was found to be approximately 6, which indicated that the use of an excess amount of THF will form the ethereal ylide predominantly even in the presence of alcohols.



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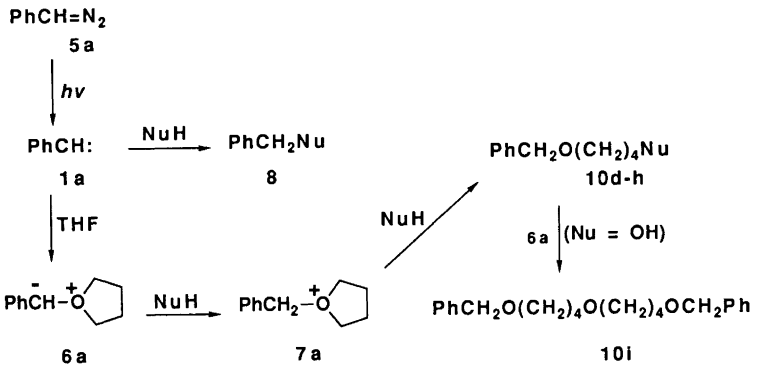
\# This paper is dedicated to Professor Lars Skattebøl who celebrated his 65th birthday in July 1992.
* To whom correspondence should be addressed.

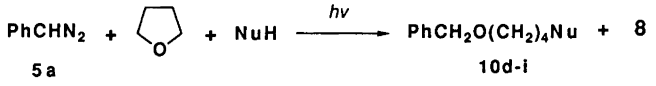


Scheme 1.

Reaction of phenylcarbene (**1b**) *with THF and a nucleophile.* On the basis of the relatively high reactivity of THF to ethoxycarbonylcarbene (**1b**), as proved above, the synthetic versatility of the one-pot ternary reactions illustrated by eqn. (1) was studied first with phenylcarbene (**1a**). Addition of an excess amount of THF to a photolysis mixture of phenyldiazomethane (**5a**) and an alcohol evidently disfavored the protonation path which, in the absence of THF, predominated to give the corresponding benzyl ether **8** analogously to the reaction of diphenyldiazomethane under similar conditions.[5,6] Results of the photolysis reactions of (**5a**) in THF in the presence of a protic nucleophile [NuH, e.g., alcohols, carboxylic acids, amines, etc., eqn. (3)] are summarized in Table 1. Ternary coupled products (**10**) were formed in low to moderate yields (20–66%) and it was independently proved that they were not the secondary photolysis products derived from the primary products. Water also reacted as a nucleophile to give **10h** and **10i**, the latter being formed by the reaction of the ylide with **10h**. The function of **10h** as a second nucleophile was confirmed independently by a reaction in which it was used as a single nucleophile.

The effect of added base, (2,6-lutidine) or added acid (acetic acid) (0.5–0.6 molar equiv. to **5a**) on the product formation was examined in the reaction of **1a** with THF in the presence of water. It was found that lutidine did not affect the product formation whereas acetic acid suppressed the formation of **10i** as well as decreasing the amount of **10h** while producing protonation product **8**. This rationally supports the idea that the key step for the formation of **10h** is the ylide formation (**6a**) and not the protonation of the carbene (Scheme 1).

Additional evidence for the preference for ylide formation over the protonation of phenylcarbene **1a** is shown in Table 1 where ternary coupled products **10** were the major products in addition to azines whereas ethers (or esters) (**8**) were not formed except with acetic acid. They



(3)

NuH: **d**, MeOH; **e**, $PhCH_2CH_2OH$; **f**, Ph-*c*-C_3H_4-CH_2OH; **g**, *c*-$C_3H_5CH(Ph)OH$; **h**, H_2O; **i**, 10h

Table 1. Photolysis reaction of phenyldiazomethane (**5a**) with THF and ROH.

Entry	ROH and additive	Diazo/ROH/Additive (mol ratio)	*t*/h	Product(s)[a]	Yield(%)[b]
1	MeOH	1/25	18	**10d**	50
2	$PhCH_2CH_2OH$	1/10	15	**10e**	66
3[c]	Ph-*c*-C_3H_4-CH_2OH	1/10	15	**10f**	36
4[d]	*c*-C_3H_5-CH(Ph)OH	1/10	15	**10g**	43
5	H_2O	1/10	20	**10h** and **10i**	20 and 10
6	**10h**	1/1	3	**10i**	37
7	H_2O, 2,6-lutidine	1/10/0.55	20	**10h** and **10i**	20 and 10
8[e]	H_2O, acetic acid	1/10/0.6	20	**10h** and **8**	13 and 12

[a] Time-dependent changes of products were analyzed by GLPC analysis. [b] Besides **10** and **8a**, azines and a considerable amount of tar-like materials were formed in most reactions. [c] ROH = 2-phenylcyclopropylmethanol. [d] ROH = cyclopropyl(phenyl)-methanol. [e] Carbene precursor **5a** did not afford **10h** or **8** under non-irradiation conditions.

present a marked contrast with the result of our separate reaction of diphenyldiazomethane where diphenylmethyl ethers were the sole products.[7]

Reaction of ethoxycarbonylcarbene (**1b**) *with THF and a nucleophile.* Ethyl diazoacetate **5b** behaved similarly [eqn. (4)] although the yields of the desired ternary coupling products (**13**) were low compared with those obtained from phenyldiazomethane;[8] some by-products such as the C–H insertion product (**18**) of THF, O–H insertion product (**9**) of ROH, and rearrangement product (**17**) were also obtained. Results are shown in Table 2. To be noted is the formation of **15** in the reaction with water where ethoxyacetic acid (**12**), which is the Wolff-rearrangement product of **1b**, was also formed. The yield of **15** increased in the reaction with 0.1 M aqueous NaOH which was added to the reaction mixture to suppress the protonation, if any. The formation of **15**, which is composed of two molecules of **1b** and one molecule each of THF and water, can be explained by the reaction sequence shown in Scheme 2 which is relevant to our working hypothesis that an ethereal oxonium ylide **6b**, and not a carbenium ion, is the key intermediate for binding three different molecules together.

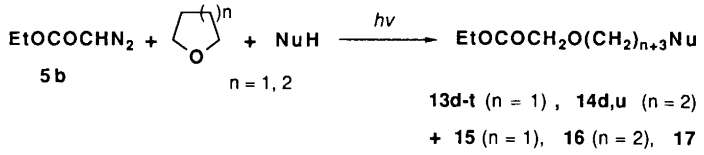
Pyrrolidine produced amides (**17v**) whereas succinimide gave **13n**. This may imply that the acidity of neutral N–H bonds (not a conjugate acid) is a more dominant factor at high pK_a values than the nucleophilicity of the nitrogen atom in the course of forming ternary coupling products **13**. Similarly, for protic nucleophiles (NuH) of low pK_a, the irradiated reactions (Table 2, entries 14–16, 19) were compared with non-irradiated ones (entries 20–23). With CF_3COOH ($pK_a = 0.23$), for example, the coupling product **13s** was obtained in 16% under irradiation whereas only a trace amount of it was afforded under dark conditions, and with *p*-toluenesulfonic acid (TsOH)[9] 11% of **13t** plus 26% of **9t** were obtained under irradiation conditions compared with 9% of **13t** besides 28% of **9t** under dark conditions. Thus, such a strong acid as TsOH evidently protonated the diazoacetate **5b** regardless of the irradiation or non-irradiation conditions whereas other acids, weaker than TsOH, shown in the table did not, and no O–H insertion product **9** was formed there. Therefore, we can conclude that the acidity of a protic nucleophile NuH controls the formation of cyclic oxonium ion **7b**, being the second key intermediate, from the corresponding ylide **6b**.

The reaction with tetrahydropyran (THP) in the presence of a nucleophile, in general, produced the coupling product in low yields[10] except the one which was carried out in the presence of water to produce **16** in 37% yield. One major reason for the low yield may be the lower reactivity of the less strained cyclic oxonioum ion (**7b**, $n = 2$) compared with the more strained alternative (**7b**, $n = 1$) towards a nucleophile. Results are also included in Table 2.

Table 2. Irradiation and non-irradiation reactions of ethyl diazoacetate (**5b**) with THF or THP and a nucleophile.

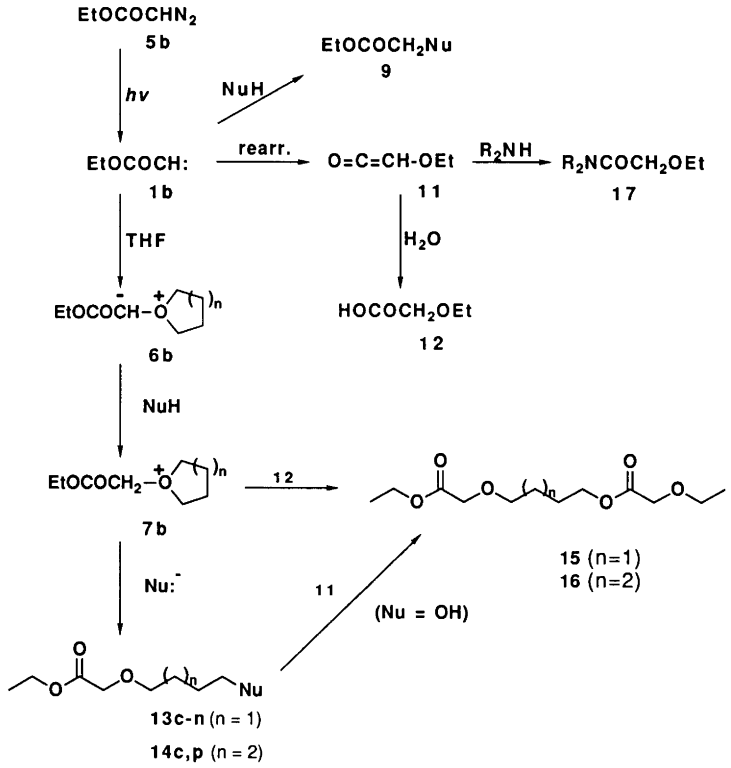
Entry	Cyclic ether	Nucleophile[a]	Product(s)[c]	Yield(%)[c]
1	THF	MeOH	**13d**	24
2	THF	MeOH[b]	**13d**	30
3	THF	$PhCH_2CH_2OH$	**13e, 9e**	61, 9
4	THF	*n*-BuOH	**13j, 18**	8, 9
5	THF	*t*-BuOH	**18**	11
6	THF	$HOCH_2CH_2OH$	**13k**	18
7	THF	$EtOCOCH_2OH$	**13m**	12
8	THF	H_2O	**15, 12**	36, 3
9	THF	0.1 M aq.NaOH	**15**	48
10	THF	Pyrrolidine	**17v**	15
11	THF	Succinimide	**13n**	20
12	THF	HCN	**13p**	10
13	THF	*n*-BuSH	**13q**	8
14	THF	$EtOCH_2COOH$	**13r**	28
15	THF	CF_3COOH	**13s**	16
16	THF	*p*-TsOH	**13t, 9t**	11, 26
17	THP	MeOH	**14d**	3
18	THP	H_2O	**16**	37
19	THP	AcOH	**14u**	16
20[d]	THF, THP	AcOH	—	—
21[d]	THF	$EtOCH_2COOH$	—	—
22[d]	THF	CF_3COOH	**13m**	0.5>
23[d]	THF	*p*-TsOH	**13n, 9n**	9, 28

[a] Molar ratio of nucleophile/diazoacetate = 2.0 in THF or THP solution, irradiation time 4 h, $T = 0°C$. [b] 2,6-Lutidine (15% to diazoacetate) was added. [c] C–H Insertion product of THF (**18**) and O–H insertion product **9** were also formed in minor amounts. Besides identified products a considerable amount of tar-like material was always formed. [d] Non-irradiated control experiments with acids: $t = 4$ h, $T = 10°C$.



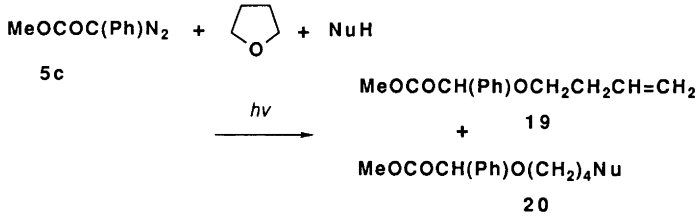
(4)

NuH: d, MeOH; e, $PhCH_2CH_2OH$; j, BuOH; k, $HOCH_2CH_2OH$; m, $EtOCOCH_2OH$; n, succinimide; p, HCN; q, BuSH; r, $EtOCH_2COOH$; s, CF_3COOH; t, *p*-TsOH; u, AcOH



Scheme 2.

Reaction of methoxycarbonyl(phenyl)carbene (**1c**). The reaction with THF of methoxycarbonyl(phenyl)carbene (**1c**) generated photolytically from methyl diazo(phenyl)-acetate (**5c**) provided a further evidence for the formation of the ethereal ylide (**6c**) [eqn. (5) and Scheme 3]. In the presence of MeOH or di(isopropyl)amine, methyl 2-phenyl-3-oxahept-6-enoate (**19**) which is a binary coupling product of the carbene with THF was obtained in moderate yields (37–44%), but neither the ternary coupling product nor the C–H insertion product was formed although both were usually formed in the reactions of **1b** with THF as shown above.[11] However, in the presence of acetic acid a ternary coupling product **20**, a similar product to **13**, was obtained (57%). The difference between the outcome of **6c** and **6b**, i.e., the observation of intramolecular 1,4-proton transfer only for **6c**, seems somewhat difficult to explain. A plausible explanation is that **6c** possesses a higher positive charge at the oxonium center because the vicinal negative charge is more delocalized in **6c** than in **6b**. Therefore, the methylene proton β to



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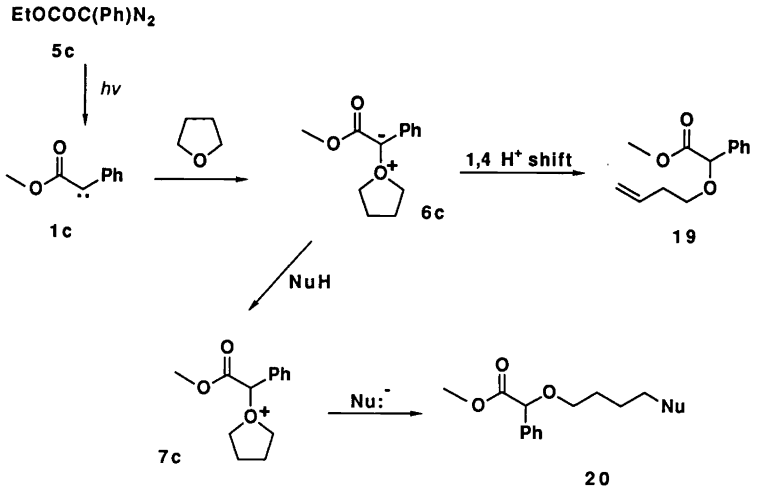

Scheme 3.

the cationic center will exhibit a lower pK_a value than that of **6b**, thus the intramolecular proton transfer would favor a β-elimination-type cleavage of the THF ring over the intermolecular protonation by a nucleophile.[12] The mechanistic preference described above for **6c** is also seen in the relatively high yield of the ternary coupling product **20**. The reaction sequence is depicted in Scheme 3.

Conclusion. Three-component coupling reactions of carbenes with a cyclic ether and a nucleophile to combine two different substituents at both termini of a polymethylene chain can be realized with phenylcarbene, ethoxycarbonylcarbene and ethoxycarbonyl(phenyl)carbene. However, the reaction profile varies mainly depending on the acidity of a protic nucleophile used and, more or less, on the structure of carbenes; we propose, at least, that their electrophilicity is more important than their proton affinity. Ethoxycarbonylcarbene seems to be a good example to distinguish several competing routes, i.e., ylide formation leading to the three-component coupling product, insertion to the α–C–H bond of the ether, insertion to the O–H bond of a nucleophile, rearrangement of the carbene to ethoxyketene, and protonation of the carbene or its precursor by an acid. To summarize, the intermediacy of cyclic ethereal oxonium ylides has been demonstrated in the reaction of carbenes (**1a–c**) with THF or THP and their synthetic utility in the forms of three-component coupling products has been presented.

Experimental

General. ^{1}H NMR spectra were recorded on a 200 MHz FT spectrometer (Varian XL-200) unless otherwise stated and chemical shifts in $CDCl_3$ are given as δ values. Mass spectra (HRMS) by the chemical ionization (CI) method were measured on a Hitachi M-80 spectrometer, IR spectra were measured in liquid films on a JASCO IR-810 spectrometer and all strong absorption bands are shown. Capillary GC analyses were performed on Shimadzu GC-9A gas chromatograph using OV-1 (25 m) and PEG (25 m) columns. For flash column chromatography a mixed solvent of ethyl acetate–hexane was used on Wacoh-Gel C-200 or 300. For irradiation an Eikosha EHB-W1-300W medium-pressure mercury lamp was used with a Pyrex filter.

Preparation of carbene precursors and nucleophiles. Tetrahydrofuran (THF) and tetrahydropyran (THP) were dried over benzophenone–sodium ketyl and distilled each time prior to use. Phenyldiazomethane (**5a**), ethyl diazoacetate (**5b**), and methyl diazo(phenyl)acetate (**5c**) were prepared from benzaldehyde, glycine ethyl ester hydrochloride, and phenylglycine, respectively, according to the methods reported.[13]

Measurement of the relative reactivity of ethoxycarbonylcarbene to THF and 2-phenylethanol. To a mixture of THF and 2-phenylethanol which were mixed in several different molar ratios (THF: $PhCH_2CH_2OH$ = 1 : 9, 1 : 3, 1 : 0.9, 1 : 0.6, 1 : 0.30, 1 : 0.15 and 1 : 0.07) to constitute an overall 20 mmol solution in an N_2-flashed Pyrex tube was placed ethyl diazoacetate (**5b**, 116 mg, 1.0 mmol). After irradiation of the solution with a medium-pressure mercury lamp for 15 h, the product mixture was analyzed by a capillary VPC using the internal standard method to determine the products **13e** and **9e**. By plotting the molar ratio **13e**/(**13e** + **9e**) vs. the ratio of initial reactant concentrations $[THF]_0/([2\text{-phenylethanol}]_0 + [THF]_0)$, the relative reactivity of 2-phenylethanol vs. THF was found to be approximately 6.0.

General procedure for the photolysis reaction of phenyldiazomethane (**5a**) *with THF. Spectroscopic data of coupling products* **10**. In a Pyrex tube (25 ml) were placed **5a** (1.0 mmol, 465 μl), THF (10 ml) and a nucleophile (for molar ratios see Table 1) and the tube was evacuated. The tube was bound to the cooling jacket of a mercury

lamp and immersed in a cooling bath maintained at 0–3°C. After the tubes had been irradiated for 15–20 h (for the exact time see Table 1), the reaction mixture was worked and the products separated on a silica gel column using EtOAc–hexane as the eluent.

1-Phenyl-2,7-dioxaoctane (**10d**). ^{1}H NMR (60 MHz, CCl_4): δ 1.50–1.80 (4 H, m), 3.22 (3 H, s), 3.20–3.53 (4 H, m), 4.20 (2 H, s).

1,9-Diphenyl-2,7-dioxanonane (**10e**). ^{1}H NMR (60 MHz, CCl_4): δ 1.47–1.83 (4 H, m), 2.78 (2 H, t, J 7.0), 3.13–3.73 (6 H, m), 4.40 (2 H, s), 7.13–7.23 (10 H, m). IR: 1600, 1500, 1450, 1360, 1100, 740, 700 cm^{-1}. HRMS(CI): m/z 284.1792 ($M+1$). Calc. for $C_{19}H_{24}O_2$: 284.1777.

1-(2-Phenylcyclopropyl)-8-phenyl-2,7-dioxaoctane (**10f**). ^{1}H NMR: δ 0.86–1.06 (2 H, m), 1.32–1.52 (H, m), 1.62–1.90 (5 H, m), 3.32–3.60 (6 H, m), 4.51 (2 H, s), 7.04–7.44 (10 H, m). IR: 1610, 1500, 1460, 1365, 1100, 740, 700 cm^{-1}.

1,8-Diphenyl-1-cyclopropyl-2,7-dioxaoctane (**10a**). ^{1}H NMR: δ 0.20–0.72 (4 H, m), 1.08–1.24 (H, m), 1.62–1.76 (4 H, m), 3.29–3.40 (2 H, t), 3.40–3.54 (2 H, t), 3.64 (H, d, J 8.0), 4.49 (2 H, s), 7.14–7.44 (10 H, m). IR: 1500, 1450, 1090, 1030, 740, 700 cm^{-1}. Anal. $C_{21}H_{26}O_2$: C, H.

4-Benzyloxybutan-1-ol (**10h**). ^{1}H NMR: δ 1.60–1.68 (4 H, m), 3.51 (2 H, t, J 5.8), 3.63 (2 H, t, J 6.4), 3.65 (1 H, s), 4.50 (2 H, s), 7.26–7.42 (5 H, m). IR: 3650–3100 (br), 2930, 2850, 1100, 1060 cm^{-1}.

1,13-Diphenyl-2,7,12-trioxatridecane (**10i**). ^{1}H NMR: δ 1.61–1.71 (8 H, m), 3.40 (4 H, t, J 4.2 Hz), 3.48 (4 H, t, J 6.2), 4.50 (4 H, s), 7.22–7.40 (10 H, m). IR: 2960, 2925, 1090 cm^{-1}.

General procedure for the photolysis reaction of ethyl diazoacetate (**5b**) *with THF and THP. Spectroscopic data of coupling products* **13**, **14**, *and* **15**. The photolysis and work-up procedures were analogous to those described above for **5a**. The molar ratios of **5b** (2.2 mmol per nucleophile) were fixed at 0.50 in 10 ml of THF or THP and irradiation times were 4 h through all the reactions. In the reactions with butanols C–H insertion products [10] were also formed (9–11%).

1-Ethoxycarbonyl-2,7-dioxaoctane (**13d**). ^{1}H NMR: δ 1.24 (3 H, t, J 7.1), 1.58–1.69 (4 H, m), 3.28 (3 H, s), 3.37 (2 H, t, J 6.0), 3.51 (2 H, t, J 6.0), 4.03 (2 H, s), 4.18 (2 H, q, J 7.1). IR: 1755, 1200, 1140, 1120 cm^{-1}. HRMS(CI): m/z 191.1286 ($M+1$). Calc. for $C_9H_{19}O_4$: 191.1286.

1-Ethoxycarbonyl-2,7-dioxaundecane (**13j**). ^{1}H NMR: δ 0.88 (3 H, t, J 8.0), 1.21–1.42 (2 H, m), 1.25 (3 H, t, J 7.2), 1.43–1.56 (2 H, m), 1.58–1.70 (4 H, m), 3.37 (2 H, t, J 6.4), 3.40 (2 H, t, J 6.0), 3.52 (2 H, t, J 6.4), 4.04 (2 H, s), 4.19 (2 H, q, J 7.2). IR: 2950, 2870, 1760, 1200, 1140 cm^{-1}. HRMS(CI): m/z 233.1742 ($M+1$). Calc. for $C_{12}H_{25}O_4$: 233.1751.

10-Oxo-3,8,11-trioxatridecan-1-ol (**13k**). ^{1}H NMR: δ 1.25 (3 H, t, J 7.2), 1.62–1.72 (4 H, m), 2.19 (H, s), 3.44–3.71 (6 H, m), 4.03 (2 H, s), 4.19 (2 H, q, J 7.2). HRMS(CI): m/z 221.1394 ($M+1$). Calc. for $C_{10}H_{21}O_5$: 221.1388.

4,13-Dioxo-3,6,11,14-tetraoxahexadecane (**13m**). ^{1}H NMR: δ 1.25 (6 H, t, J 7.8), 1.63–1.74 (4 H, m), 3.53 (4 H, t, J 6.4), 4.03 (4 H, s), 4.20 (4 H, q, J 7.8). HRMS(CI): m/z 263.1501 ($M+1$). Calc. for $C_{12}H_{23}O_6$: 263.1493.

4,12-Dioxo-3,6,11,14-tetraoxahexadecane (**15**). ^{1}H NMR: δ 1.17 (3 H, t, J 7.2), 1.21 (3 H, t, J 7.4), 1.51–1.78 (4 H, m), 3.48 (2 H, t, J 6.0), 3.51 (2 H, t, J 7.2), 3.95 (2 H, s), 4.00 (2 H, s), 4.12 (2 H, t, J 6.1), 4.14 (2 H, q, J 7.4). IR: 1755, 1735, 1205, 1140 cm^{-1}. Anal. $C_{12}H_{23}O_6$: C, H.

Ethyl 3,9-dioxadecanoate (**14d**). ^{1}H NMR: δ 1.26 (3 H, t, J 7.2), 1.35–1.50 (2 H, m), 1.50–1.70 (4 H, m), 3.31 (3 H, s), 3.36 (2 H, t, J 6.8), 3.51 (2 H, t, J 6.6), 4.04 (2 H, s), 4.20 (2 H, q, J 7.2). IR: 2950, 2870, 1755, 1200, 1140 cm^{-1}. HRMS(CI) m/z 205.1444 ($M+1$). Calc. for $C_{10}H_{21}O_4$: 205.1440.

2,11-Dioxo-3,9,12-trioxatetradecane (**14u**). ^{1}H NMR (60 MHz, CCl_4): δ 1.27 (3 H, t, J 7), 1.33–1.77 (6 H, m), 2.00 (3 H, s), 2.47 (2 H, t, J 6), 3.93 (2 H, s), 4.00 (2 H, t, J 7), 4.17 (2 H, q, J 7). IR: 2950, 1740, 1440, 1370, 1240, 1200, 1140, 1040 cm^{-1}. HRMS(CI): m/z 233.1407 ($M+1$). Calc. for $C_{11}H_{21}O_5$: 233.1388.

Reaction of **5b** *with THF in the presence of nucleophiles other than alcohols.*

Ethyl 4-(2,5-dioxopyrrolidin-3-yl)butoxyacetate (**13n**). ^{1}H NMR: δ 1.27 (3 H, t, J 7.2), 1.52–1.74 (4 H, m), 2.68 (4 H, s), 3.52 (4 H, t, J 6.0), 4.03 (2 H, s), 4.19 (2 H, q, J 7.2). IR: 2950, 1750, 1700, 1440, 1405, 1375, 1345, 1300, 1255, 1210, 1170, 1140, 1030 cm^{-1}. HRMS(CI): m/z 258.1340 ($M+1$). Calc. for $C_{12}H_{20}NO_5$: 258.1340.

Ethyl 7-cyano-3-oxaheptanoate (**13p**). ^{1}H NMR: δ 1.29 (3 H, t, J 7.3), 1.70–1.85 (4 H, m), 2.45 (2 H, t, J 7.0), 3.57 (2 H, t, J 5.8), 4.05 (2 H, s), 4.20 (2 H, q, J 7.3). IR: 2975, 2230, 1760, 1210, 1140 cm^{-1}. HRMS(CI): m/z 186.1135 ($M+1$). Calc. for $C_9H_{16}NO_3$: 186.1131.

Ethyl 7-butylthio-3-oxaheptanoate (**13q**). ^{1}H NMR: δ 0.89 (3 H, t, J 7.2), 1.27 (3 H, t, J 7.2), 1.28–1.61 (4 H, m), 1.66–1.80 (4 H, m), 2.43–2.62 (2 H, br), 3.55 (2 H, t, J 6.2), 4.04 (2 H, s), 4.20 (2 H, q, J 7.2). IR: 2940, 1760, 1200, 1140 cm^{-1}. HRMS(CI): m/z 248.1444 ($M+1$). Calc. for $C_{12}H_{24}O_3S$: 248.1444.

4,12-Dioxo-3,6,11,14-tetraoxahexadecane (**13r**). ^{1}H NMR: δ 1.17 (3 H, t, J 7.2), 1.21 (3 H, t, J 7.4), 1.51–1.78 (4 H, m), 3.48 (2 H, t, J 6.0), 3.51 (2 H, q, J 7.2), 3.95 (2 H, s), 4.00 (2 H, s), 4.12 (2 H, t, J 6.1), 4.14 (2 H, q, J 7.4). IR: 1755, 1735, 1205, 1140 cm^{-1}. LRMS(CI): m/z 263 ($M+1$), 159 (P). Anal. $C_{12}H_{22}O_6$: C, H.

Ethyl 7-trifluoroacetoxy-3-oxaheptanoate (**13s**). ^{1}H NMR: δ 1.24 (3 H, t, J 7.2), 1.59–1.94 (4 H, m), 3.53 (2 H, t, J 5.8), 4.03 (2 H, s), 4.17 (2 H, q, J 7.2), 4.37 2 H, t, J 6.5). IR: 2950, 1795, 1790, 1220, 1160, 1035 cm^{-1}. HRMS(CI): m/z 273.0946 ($M+1$). Calc. for $C_{10}H_{16}F_3O_5$: 273.0948. Anal. $C_{10}H_{16}F_3O_5$: C, H, F.

*Ethyl 7-(*p*-tolylsulfonyloxy-3-oxaheptanoate* (**13t**). ^{1}H NMR: δ 1.24 (3 H, t, J 7.2), 1.52–1.81 (4 H, m), 2.41 (3 H, s) 3.54 (2 H, t, J 5.9), 3.97 (2 H, s), 4.05 (2 H, t, J 6.2), 4.17 (2 H, q, J 7.2), 7.33 (2 H, d, J 9.2), 7.75 (2 H, d, J 9.2). IR: 2960, 1760, 1600, 1450, 1360, 1295, 1145, 1100, 1020, 940 cm^{-1}. LRMS: m/z 331 ($M+1$), 159 (P).

Ethyl 7-acetoxy-3-oxaheptanoate (**13u**). ^{1}H NMR: δ 1.26 (3 H, t, J 7.3), 1.62–1.77 (4 H, m), 2.02 (3 H, s), 3.54 (2 H, t, J 6.0), 4.05 (2 H, s), 4.08 (2 H, t, J 6.2), 4.20 (2 H, q, J 7.3). IR: 2960, 1745, 1370, 1245, 1205, 1140, 1035 cm^{-1}.

N,N-*Tetramethylene(ethoxy)acetamide* (**17v**). ^{1}H NMR: δ 1.09 (3 H, t, J 7.2), 1.71–1.97 (4 H, m), 3.38 (2 H, t, J 6.7), 3.44 (2 H, t, J 6.8), 3.54 (2 H, q, J 7.2), 4.02 (2 H, s). IR: 2975, 2875, 1650, 1120 cm^{-1}. HRMS(CI): m/z 158.1182 ($M+1$). Calc. for $C_8H_{16}NO_2$: 158.1180.

Ethoxyacetamide (**17w**). ^{1}H NMR: δ 1.21 (3 H, t, J 7.1), 3.55 (2 H, q, J 7.1), 3.90 (2 H, s), 6–7 (2 H, br). IR: 3425, 3200, 2980, 2900, 1760, 1660, 1430, 1340, 1120 cm^{-1}. HRMS(CI): m/z 104.0707 ($M+1$). Calc. for $C_4H_{10}NO_2$: 104.0710.

N-*Phenyl(ethoxy)acetamide* (**17x**). ^{1}H NMR (60 MHz, CCl_4): δ 1.32 (3 H, t, J 7.0), 3.71 (2 H, q, J 7.0), 4.00 (2 H, s), 7.06–7.77 (5 H, m). IR: 3400, 2990, 1690, 1605, 1530, 1445, 1310, 1120, 760, 700 cm^{-1}. HRMS(CI): m/z 179.0939 ($M+1$). Calc. for $C_{10}H_{13}NO_2$: 179.0945.

*Ethyl (*p*-tolylsulfonyloxy)acetate* (**9t**). ^{1}H NMR (60 MHz, CCl_4): δ 1.35 (3 H, t, J 7.5), 2.54 (3 H, s), 4.20 (2 H, q, J 7.5), 4.48 (2 H, s), 7.36 (2 H, d, J 8.0), 7.79 (2 H, d, J 8.0).

Photolysis reaction of ethyl diazo(phenyl)acetate (**5c**) *with THF.* The procedures were analogous to that described above for (**5a**). The molar ratios of **5c** (2 mmol per nucleophile) were fixed at 1 : 3 in 10 ml of THF but the irradiation times varied in the range 1–4 h.

Methyl 2-phenyl-3-oxahept-6-enoate (**19**). ^{1}H NMR: δ 2.41 (2 H, q, J 6.8), 3.49 (H, dt, J 9.1, 6.8), 3.58 (H, dt, J 9.1, 6.8), 3.71 (3 H, s), 4.88 (H, s), 5.03 (H, d, J 10.2), 5.08 (H, d, J 16.0), 5.82 (H, ddt, J 16.0, 10.2, 6.8), 7.29–7.56 (5 H, m). IR: 2960, 1760, 1545, 1500, 1460, 1440, 1270, 1215, 1180, 1125, 1080, 1035, 920, 735, 700 cm^{-1}. HRMS(CI): m/z 221.1180 ($M+1$), Calc. for $C_{13}H_{17}O_3$: 221.1176.

Methyl 2-phenyl-7-acetoxy-3-oxaheptanoate (**20**). ^{1}H NMR (60 MHz, CCl_4): δ 1.52–2.00 (4 H, m), 2.00 (3 H, s), 3.33–3.62 (2 H, m), 3.67 (3 H, s), 4.09 (2 H, t, J 7), 4.75 (H, s), 7.15–7.60 (5 H, m). HRMS(CI): m/z 281.1375 ($M+1$). Calc. for $C_{15}H_{21}O_5$: 281.1383.

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