Tetrahedron xxx (2016) 1–10

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Radical additions of acyclic and cyclic ethers to alkenes via an allyl transfer reaction involving phthalimido-*N*-oxyl radical

Shradha V. Patil, James M. Tanko *

Virginia Polytechnic Institute and State University, Department of Chemistry, Blacksburg, 24061, USA

ARTICLE INFO

Article history:
Received 28 March 2016
Received in revised form 13 May 2016
Accepted 16 May 2016
Available online xxx

Keywords:
Ether functionalization
Phthalimido-N-oxyl radicals
Chain reaction
Allyl transfer
C–H bond

ABSTRACT

Direct functionalization of rudimentary and cheap starting materials to yield complex value added products is of great interest to synthetic chemists. Particularly, direct functionalization of cheap commodity molecules that have been traditionally considered inert to known reactions are of widespread interest. We have previously demonstrated the functionalization of benzylic C–H bonds via an allyl transfer reaction using various allyl-phthalimido-*N*-oxyl substrates. In this work, we demonstrate the extension of our mild, metal-free, and neutral allyl transfer methodology to the direct functionalization of ethers. The C–H bond in α position to the ether oxygen in various acyclic and cyclic ethers was functionalized in high yields demonstrating wide substrate scope for this transformation. Furthermore, selective mono-functionalization of symmetrical cyclic ethers and regioselective functionalization of unsymmetrical ethers was achieved, thus demonstrating further utility of this reaction. Finally, kinetic chain length measurements were performed, which provided valuable insights into the initial rates and efficiency of the chain process involving the phthalimido-*N*-oxyl (PINO•) radical.

1. Introduction

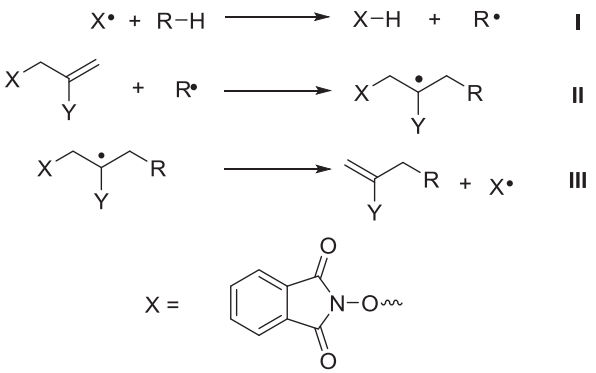
The direct C–H bond activation and functionalization reactions are fascinating to organic chemists, as they provide easily accessible, economical, and novel routes for interesting synthetic applications. Various high efficiency and versatile methods have been reported for such activations and functionalization reactions.[1] These reactions can be categorized mainly into: 1) sp^2 α-C–H reactions of arene, alkene, aldehyde, imine;[2] 2) sp^3 α-C–H reactions of allyl, benzyl, carbonyl compounds;[3] 3) sp^3 α-C–H reactions of heteroatomic compounds containing oxygen, nitrogen and sulfur.[4] The third type, sp^3 α-C–H activation followed by C–C bond formation in reactions of alcohols, ethers, and amines is quite useful because of the direct conversion of these relatively inert compounds into substrates of varying complexity. This article summarizes our successful efforts in developing a method of sp^3 α-C–H activation and ether functionalization via an allyl transfer reaction.

The addition-elimination reactions of carbon-centered radicals generated from ethers via α-C–H activation-functionalization have been extensively studied, particularly for cyclic ethers.[2b,5] Examples include radical addition-elimination reaction of THF with alkenyl or alkynyl triflones leading to α-acetylenic ethers,[6] alkenylation of THF with 1,2-disubstituted vinyl triflones leading to α-vinyl products,[6c] reactions of THF with polyfluoro-alkenes to synthesize α-polyfluoroalkyl ethers, NHPI (*N*-hydroxyphthalimide)/$Co(OAc)_2$ catalyzed radical addition of ethers to alkenes,[7] radical addition of alcohols to the alkynes using TBHP (tributyl hydroperoxide) to yield corresponding allylic alcohols,[8] and finally, radical additions using initiator BEt_3/O_2 or Me_2Zn/O_2 leading to the formation of hydroxy alkyl ethers.[9]

In earlier studies, we devised a free radical-based chain reaction that achieves hydrocarbon functionalization and C–C bond formation[10] that achieves the overall conversion $R\text{-}H + CH_2{=}C(Z)CH_2X \rightarrow RCH_2C(Z){=}CH_2 + H\text{-}X$ (where X=Br or more recently, the *N*-hydroxyphthalimide radical, abbreviated as PINO). The mechanism for this reaction is depicted in Scheme 1.[10c] In developing this process, several known radical reactions (hydrogen atom abstraction, radical additions to unsaturated centers, and β-cleavage)[11] were tailored to achieve the desired overall conversion. Initially, the substrates were limited to allyl bromides (where bromine atom was the chain carrier) and benzylic hydrocarbons (e.g., toluene, ethyl benzene, cumene, owing to their weak C–H bond, BDE 88–92 kcal).[12] More recently, we were able to replace the Br with PINO, which produces the by-product *N*-hydroxyphthalimide (NHPI). Quite conveniently, NHPI precipitates out of solution eliminating the need for an HBr scavenger, and making the work-up particularly easy and convenient).[10a,10c]

* Corresponding author. Tel.: +1 540 231 6687; fax: +1 540 231 3255; e-mail address: jtanko@vt.edu (J.M. Tanko).

http://dx.doi.org/10.1016/j.tet.2016.05.046
0040-4020/



Scheme 1. Allyl transfer reaction for hydrocarbon functionalization.

Since the bond dissociation energies of ethers and acetals are comparable to benzylic hydrocarbons, we reckoned that this allyl transfer chemistry could be adapted to a new class of substrates. Moreover, because acetals are essentially protected aldehydes, it was thought that we could further develop this allyl transfer chemistry using acetals as acyl radical equivalents.

2. Results and discussion

2.1. Introduction to ether functionalization via allyl transfer

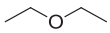
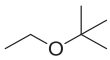
Similar to benzylic hydrocarbons, ethers have weak α-C—H bonds[13] (THF, BDE 93.8 kcal/mol; 1,3-dioxane, BDE 93.3 kcal/mol) owing to the resonance stabilization of resulting radical **2** by the vicinal oxygen atom (Fig. 1). Ethers are thus a suitable choice as substrates for H-abstraction, and in this paper, we comprehensively discuss the method of α-alkoxyl C—H bond functionalization via allyl transfer using phthalimido-*N*-oxyl radical (PINO•). As hoped, the reaction proceeds via the abstraction of α-hydrogen from ether, with the subsequent addition/elimination of the carbon radical to allyl-PINO substrates (Scheme 1).

Fig. 1. Resonance stabilization of α-alkoxyl radical derived from tetrahydrofuran (THF).

2.2. Direct functionalization of acyclic ethers via allyl transfer

The reactions of acyclic ethers (diethyl ether and *tert*-butyl ethyl ether) with allyl-PINO substrates **3** and **4** were performed at 120 °C in sealed pressure tubes (Scheme 2). The precipitation of the side product, NHPI, as a white solid helped recycle it making this a cost effective synthetic method. The data in Table 1 reports the isolated and GC yields of these reactions, and shows that the reactions of diethyl ether and *tert*-butyl ethyl ether (both of which possess equivalent reactive hydrogen atoms) led to products **5**, **6**, and **7**, and **8**, respectively in high (up to 90%) yields (see Supplementary data S2 and S6 for characterization).

Table 1
Functionalization of acyclic ethers via allyl transfer reaction

Entry[a]	Ether	Z[b]	Time (h)	Product	Isolated yield (%)	GC yield (%)
1		CO_2Et	4	**5**	83	90
2		Ph	24	**6**	85	90
3		CO_2Et	4	**7**	85	90
4		Ph	24	**8**	85	90

[a] DTBPO=0.07 M, ether as solvent.
[b] Allyl-PINO substrate=0.45 M.

2.3. Direct functionalization of cyclic ethers

In conjunction with our work on acyclic ethers, we speculated that the same functionalization would be possible with cyclic ethers and thioethers. Cyclic ethers such as tetrahydrofuran (THF), 2-MeTHF are key structural motifs in a large number of biologically active compounds and natural products.[14] Thus, direct functionalization of these substrates using allyl transfer chemistry would provide the basis for a new and useful synthetic method.[15] We screened a set of ethers such as THF, THP (tetrahydropyran), 1,4-dioxane, THT (tetrahydrothiophene) and 1,3-benzodioxole in the allyl transfer reaction with substrates **3** and **4**. The conditions for these reactions are similar to those described above. And, as was the case for the acyclic ethers, these compounds have only one functionalizable C—H bond owing to its symmetry. The observed products for these reactions are shown in Fig. 2 (see Supplementary data S2 for spectral data).

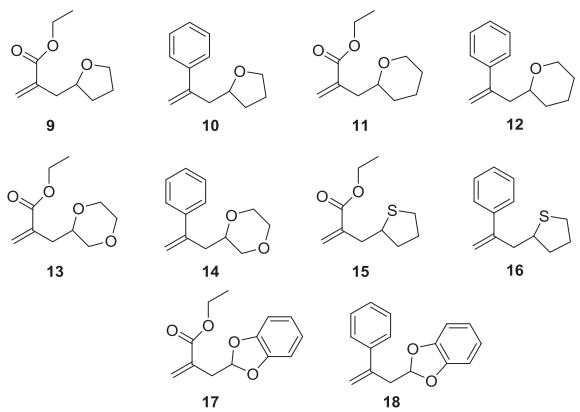
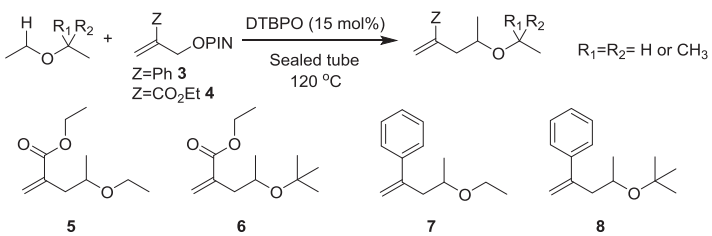


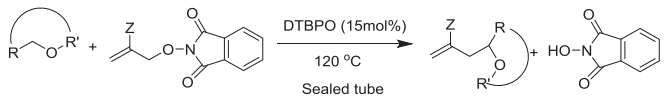
Fig. 2. Products arising from reactions of cyclic ethers and thioether with ally-PINO substrates **3** and **4**.



Scheme 2. Functionalization of acyclic ethers; ethyl ether and *tert*-butyl ethyl ether via allyl transfer reactions (DTBPO=di-*tert*-butyl peroxide).

Table 2 reports the results of cyclic ether and thioether functionalization. In the case of THF (entries 1, 2), the observed yield was slightly lower than the other ethers possibly due to further addition of reactive THF radical to the product alkene especially when Z=CO_2Et. Although this phenomenon was not prominently observed in other cases, trace impurities analysis using MS confirmed this further addition. High isolated yields were observed for reactions of THP and 1,4-dioxane (entries 3–6). THT (entries 7, 8) could also be easily functionalized using this method. Similarly, the 1,3-benzodioxole (entries 9,10), which is an important building block for biologically active heterocycles, was also functionalized using this method.

Table 2
Functionalization of cyclic ethers and benzo-1,3-dioxole via allyl transfer reaction[a]



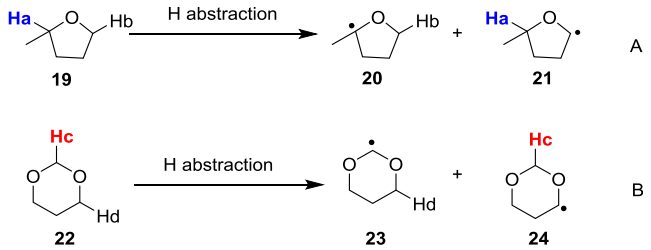
Entry	Ether	Z	Time (h)	Product	Isolated yield (%)	GC yield (%)
1		CO_2Et	1	**9**	60	65(±3)
2		Ph	16	**10**	75	70(±2)
3		CO_2Et	2	**11**	85	85(±3)
4		Ph	16	**12**	84	90(±2)
5		CO_2Et	1	**13**	88	88(±2)
6		Ph	18	**14**	85	90(±1)
7		CO_2Et	2	**15**	85	88(±1)
8		Ph	18	**16**	85	90(±2)
9		CO_2Et	8	**17**	80	86(±3)
10		Ph	14	**18**	75	81(±2)

[a] (Sealed tube, 120 °C, 3, **4**=0.45 M, DTBPO=0.007 M, ether as solvent).

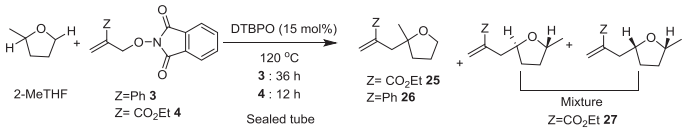
2.4. Competition for H-abstraction in 2-MeTHF and 1,3-dioxane

Cyclic ethers such as 2-MeTHF and 1,3-dioxane, which are unsymmetrical and thus have more than one functionalizable α-hydrogen atoms, were also studied. In these cases, we feared that the allyl transfer reaction might lead to multiple products, owing to the competition in hydrogen abstraction.

For example, in the case of 2-MeTHF **19**, abstraction of H_a leads to a tertiary radical **20**, whereas abstraction of H_b leads to a secondary radical **21**. Thus, we expected reasonably good chemoselectivity for reactions of 2-MeTHF since **20** is expected to be more stable than **21**. In case of 1,3-dioxane **22**, both hydrogens (H_c and H_d) are secondary leading to radicals **23** and **24**, and thus, lower chemoselectivity was anticipated (see Schemes 3 and 4).



Scheme 3. Competition for H abstraction in A) 2-MeTHF, B) 1,3-dioxane.



Scheme 4. Functionalization of 2-MeTHF via allyl transfer reaction.

2.5. Functionalization of 2-MeTHF via allyl transfer reaction

Table 3 reports the results of the reaction of 2-MeTHF with allyl-PINOs **3** and **4**. For the reaction in entry 1, Gas chromatographic analysis was conducted to calculate the relative ratios of **28** to **26** and **25** to **27** shown in Fig. 2. Analysis by GC revealed three products were formed in this reaction. The major product is (80%) is **26**, whereas the minor products are cis- and trans-**28** formed in 20% yield. These assignments were confirmed using ^{1}H NMR analysis in which methyl protons from the major product appear as a singlet at 1.12, whereas methyl protons from the cis and trans isomers of **28** appear as doublets at 1.20 and 1.25 (see Supplementary data, Fig. S9 and S10) (see Fig. 3).

Table 3
Functionalization of 2-MeTHF via allyl transfer reaction

Entry	Substrate	Time (h)	Overall yield (%)	Product	GC yield (%)	Integrated NMR yield (%)
1[a]	3	36	80	**26**	80	79
				28(cis+trans)	20	21
2[a]	4	12	82	**25**	—	70
				27(cis+trans)		30

[a] Reactions were performed in sealed pressure tubes using neat 2-MeTHF and di-*tert*-butyl peroxide (15 mol %), (Sealed tube, 120 °C) (**3**, **4**=0.4 M, DTBPO=0.06 M, 2-MeTHF=10.0 M).

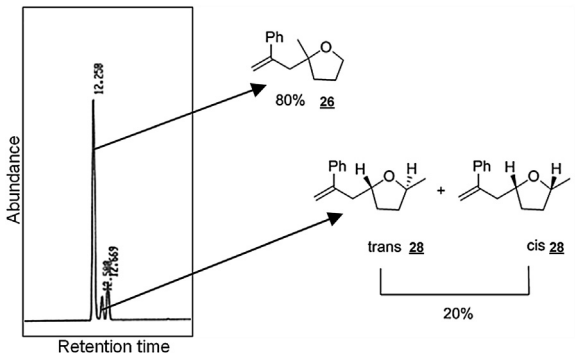
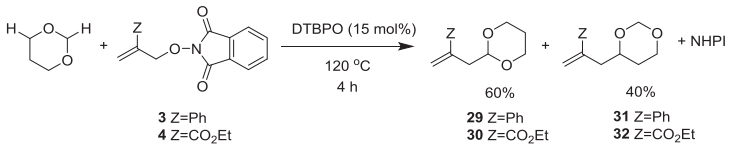


Fig. 3. GC analysis of 2-MeTHF functionalization showing all regioisomeric products.

Please cite this article in press as: Patil, S. V.; Tanko, J. M., Tetrahedron (2016), http://dx.doi.org/10.1016/j.tet.2016.05.046

2.6. Functionalization of 1,3-dioxane via allyl transfer reaction

As mentioned above, similar to 2-MeTHF, 1,3-dioxane also has multiple functionalizable C–H bonds. The functionalization of 1,3-dioxane was performed using di-*tert*-butyl peroxide (15 mol %) in neat 1,3-dioxane. This reaction led to the formation of a mixture of products as shown in Scheme 5. The ratio of products in this case was measured using ^{1}H NMR spectroscopy. A close competition in hydrogen abstraction was observed in this case that led to major: minor (**29**: **30**) product ratio of 60: 40 (Scheme 5) (see Supplementary data S2) (see Table 4).



Scheme 5. Functionalization of 1,3-dioxane via allyl transfer reaction.

Table 4
Allyl transfer reaction of 1,3-dioxane leading to mixture of products

Entry[a]	Substrate	Time (h)	Overall reaction yield (%)	Products	Integrated NMR yield (%)
1	**3**	4	88	**29**	60
				31	40
2	**4**	24	85	**30**	62
				32	38

[a] (Sealed tube, 120 °C) (**4**=0.4 M, DTBPO=0.06 M, 1,3-dioxane=10.0 M).

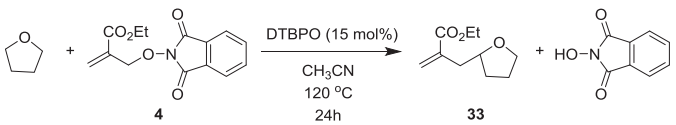
As anticipated, the low regioselectivity arises because the C-H bond strength of both hydrogen atoms (H_c and H_d) is nearly identical, 93.3 and 93.8 kcal/mol,[18] respectively (Scheme 3).

2.7. Allyl transfer in solution using low concentration of reagents

One of the drawbacks of these allyl transfer reactions is the need to use high concentrations of substrate, i.e., the ether was used as both a substrate and a solvent. The versatility of this reaction would be vastly improved if it were possible to use significantly lower concentrations of substrate, in an inert solvent such as acetonitrile. As a test, we examined the reaction of various concentrations of THF with allyl-PINO compound **4** in acetonitrile solvent. As the results in Table 5 demonstrate, decreasing the THF concentration does not adversely impact the overall yield until there are less than 3 equiv of THF present. These results demonstrate that these reactions can be performed using considerably lower concentrations of substrate.

Returning to the regioselectivity of the reaction of 1,3-dioxane, we speculated that the poor selectivity in hydrogen abstraction by PINO•, might be improved a) by reducing the concentration of initiator, or b) by using low concentration of 1,3-dioxane (i.e., by performing reaction in solution). The rationale was that the initiating radical (*tert*-butoxyl), which is notoriously unselective, might be playing a large role than desired in the H-atom abstraction.

Table 5
THF functionalization in solution (acetonitrile)[a]

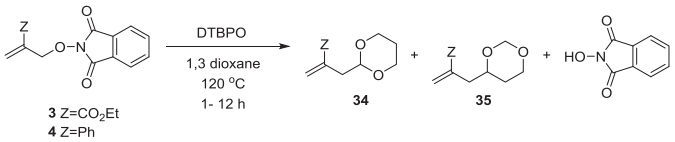


Entry	THF (equiv)	Conc. of THF (M)	Yield (%) 33
1	1	0.07	30
2	2	0.14	45
3	3	0.21	60
4	4	0.28	62
5	10	0.71	65

[a] (**4**=0.07 M, DTBPO=0.010 M).

To test this hypothesis, a series of experiments were performed at varying concentration of 1,3-dioxane. The resulting product mixture was analyzed using NMR spectroscopy to determine the ratios of the major: minor product (Table 6). As seen in entries 1 and 2, reducing the concentration of 1,3-dioxane from 18 M to 0.8 M did not improve selectivity of this reaction.

Table 6
Allyl transfer reaction in solution



Entry	Substrate	DTBPO (mol %)	1,3-Dioxane (eq.)	1,3-Dioxane (M)	GC yield (%)[a] (3–104+3–105)	Ratio (3–104:3–105)[b]
1	3	15	30	18	85	60:40
2[c]	3	15	3 in CH_3CN	0.8	66	60:40
3[c]	3	10	3 in CH_3CN	0.8	62	67:33
4	4	15	30	18	82	59:41
5[c]	4	10	3 in CH_3CN	0.8	60	66:34

[a] GC yield was calculated using internal standard diphenylmethane.
[b] Product ratios were determined using ^{1}H NMR spectroscopy.
[c] (**3**, **4**=0.07 M, DTBPO=0.010 M, THF=0.21 M).

Similarly, to test if reducing the amount of initiator (DTBPO) improved the selectivity, the concentration of initiator was reduced to 10 mol % (entry 3). However, this change did not lead to significant improvement of selectivity. A similar trend was observed when **4** was used as the substrate (entries 4 and 5).

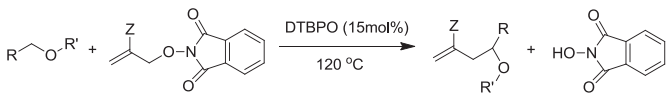
2.8. Kinetic chain length measurements

In order to learn more about the mechanistic and kinetic aspects of the ally-transfer reactions with ethers, we conducted initial kinetic chain-length measurements. To probe this, the initial kinetic chain lengths (i.e., the rate of product formation relative to the rate of initiator disappearance, $-(\partial[\text{product}]/\partial t)/(2\partial[\text{DTBPO}]/\partial t)$)[16] were determined by following product yields as a function of time for

Please cite this article in press as: Patil, S. V.; Tanko, J. M., Tetrahedron (2016), http://dx.doi.org/10.1016/j.tet.2016.05.046

Z=CO_2Et, Ph (Table 7). The data in Table 7 illustrates that the allyl transfer reactions are highly efficient chain reactions with kinetic chain lengths as high as 15,000. While the chain lengths for THF and 1,4-dioxane were both very high, the chain length was significantly shorter for 2-MeTHF. This decrease in chain length can be attributed to the competition in hydrogen abstraction and the steric crowding in the radical addition step. Although chain lengths in solution were significantly lower than the reactions with neat ethers, the results nonetheless show that it is still an efficient chain reaction in solution (see Supplementary data S3).

Table 7
Kinetic chain length data for allyl transfer reactions of ethers[a]

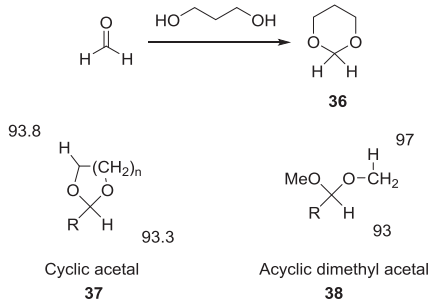


Z	THF[a]	THF[a] (3eq. In ACN)	2-MeTHF (major product)	2-MeTHF (all products: Mixture)	1,4-Dioxane
CO_2Et	15,000 (±5000)	40 (±20)	300 (±70)	1200 (±400)	8000 (±2500)
Ph	1200 (±600)	N/D	N/D	80 (±20)	1300 (±300)

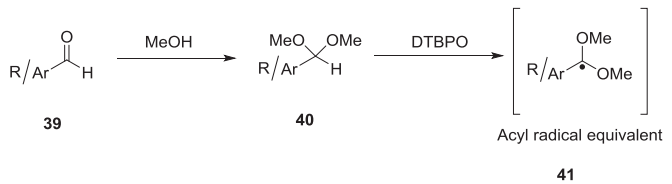
[a] (**3**, **4**=3.5 mM, DTBPO=0.53 mM).

2.9. C–H functionalization of acetals

So far we have discussed the reaction of 1,3-dioxane with allyl-PINO substrates via an allyl transfer. Since, 1,3 dioxane is a cyclic acetal of formaldehyde (**36**), we extended this work to various acetals. The results above show that the cyclic acetals (such as 1,3-dioxane) can lead to multiple products owing to the competition in hydrogen abstraction. To solve this problem, we speculated that the difference in BDEs in acyclic dimethyl acetals such as **38** might be sufficiently large that little or no H-abstraction would occur from the methoxyl group. Through the use of such acyclic dimethyl acetals, we envisioned it would be possible to generate an acyl radical equivalent in situ, which can then be used in the allyl transfer reaction (Scheme 6). To achieve this objective, we chose aromatic aldehydes which can easily undergo acetal formation reaction with methanol to yield the corresponding dimethyl acetal (see Scheme 7).

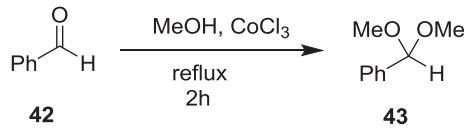


Scheme 6. Comparison of BDEs between cyclic ether and acyclic dimethyl ether.



Scheme 7. Pathway for functionalization of acyclic dimethyl acetal.

The dimethyl acetal of benzaldehyde was synthesized using a literature procedure (Scheme 8).[17] A convenient and efficient method was used for acetalization of benzaldehyde with methanol using the inexpensive and water tolerant $CoCl_2$ as a catalyst. This method did not involve strong acidic or basic conditions and the metal catalyst was recycled without the loss of activity (see Supplementary data S2 for experimental procedure, and spectral data for **43**, **45**).



Scheme 8. Acetalization of benzaldehyde using methanol in the presence of $CoCl_2$.[17]

Reactions of dimethyl acetal of benzaldehyde with **3** and **4** were optimized in such a way that minimum concentration of the ether reagents and initiator could be used (see Scheme 9).

In both cases of reactions of **43** with **3** and **4**, the expected acetyl products hydrolyzed upon work-up and high yields were observed for the desired ketone product **45** (Table 8). This type of functionalization is not known under mild and metal-free reaction conditions. The products are stable and do not isomerize to the conjugated ketone. Especially in entry 2, where the alkene double bond is not in conjugation with the ketone carbonyl does not isomerize to the α,β-unsaturated ketone isomer (see Supplementary data for spectral data).

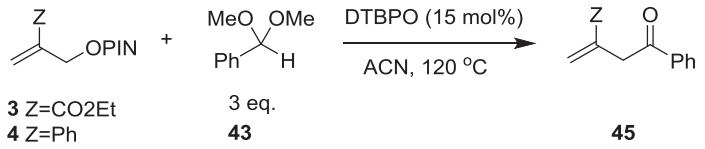
2.10. Amine C–H bond functionalization via allyl transfer

Similar to alkyl aromatic hydrocarbons and ethers, we envisioned that the allyl transfer reaction would work for the selective functionalization of α-C–H bond containing tertiary amines. Since BDEs of α-C–H bonds of amines such as triethylamine (93.9 kcal/mol) or *N*,*N*-dimethylaniline (93.1 kcal/mol) are similar to the BDEs of benzylic hydrocarbons and ethers,[18] we speculated them to undergo the same chain reaction via allyl transfer. Especially, the hydrogen abstraction from the methyl C–H bond of alkyl aromatic amines (for example, *N*,*N*-dimethylaniline) could potentially lead to the corresponding carbon radical, which is in resonance with the lone pair of the electrons on the nitrogen (Scheme 10). This stable radical might lead to the efficient allyl transfer with the appropriate substrate. Functionalization of *N*,*N*-dimethylaniline via allyl transfer was attempted as a pilot reaction.

In this experiment, an interesting result was observed along with <10% of desired product formation was recorded. Major product of the reaction was separated and identified as a dimer of *N*,*N*-dimethyl aniline (Scheme 11).

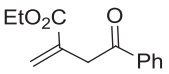
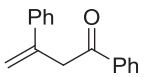
A likely mechanistic pathway for this reaction is shown in Scheme 12, where we speculate that PINO• is involved in single electron oxidation of aniline leading to aniline radical cation **49**. **49** can potentially undergo a dimerization to form the intermediate **50** which on deprotonation by PINO• undergoes re-aromatization leading to the dimer product **51**.

In 2005, Baciocchi, et al. reported a similar single electron transfer from *N*,*N*-dimethylaniline to PINO•[19] leading to demethylation of *N*,*N*-dimethylaniline (Scheme 12) This confirms that such single electron transfer pathway is possible with the alkyl aromatic amines and partially supports the proposed pathway for dimerization of *N*,*N*-dimethylaniline.

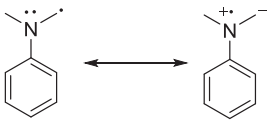


Scheme 9. Functionalization of dimethyl actetal of benzaldehyde.

Table 8
Results for the functionalization of dimethyl acetal of benzaldehyde in acetonitrile

Entry[a]	Z	Product (**45**)	Time (h)	Yield % (isolated)
1	CO_2Et		24	84
2	Ph		24	89

[a] (Sealed tube, 120 °C) (**3** and **4**=0.35 M, **43**=1.07 M, DTBPO=0.05 M).

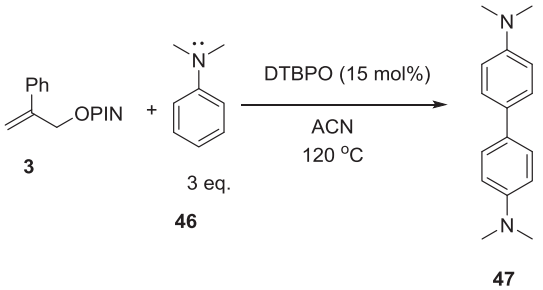


Scheme 10. Resonance stabilization of methyl radical in aniline.

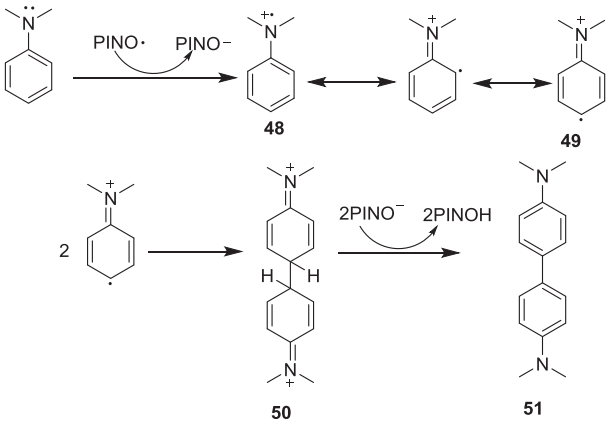
3. Conclusions

In conclusion, we have demonstrated an efficient method for functionalization of various ethers and dimethyl acetal of benzaldehyde via an allyl transfer reaction using phthalimido-*N*-oxyl radical as a chain carrier. The utility of this method is established by observed high yields and high mass balances under metal-free, mild, and neutral reaction conditions. A wide substrate scope, as established by several acyclic and cyclic ethers and acetals is demonstrated for this transformation. The reported allyl transfer reaction was successfully carried out in-solution using acetonitrile as solvent, which allowed successful implementation at low concentration of reagents, thus making this a cost-effective and environmentally friendly method of ether functionalization.

The PINO• shows good selectivity in hydrogen abstraction especially in case of 2-MeTHF, leading to 80% tertiary C—H functionalization (major product), and 20% secondary C—H functionalization (minor product). However, in case of 1,3-dioxane moderate selectivities were observed due to the competition between two active secondary C—Hs present. These two experiments provided a valuable insight into selectivity/reactivity of PINO• in hydrogen abstraction, thus helping us in designing a similar protocol with acetals, which in turn can be used as a method to allylate aldehydes. A dimethyl acetal of benzaldehyde was used to demonstrate this reaction, and high isolated yield for desired allylated aldehyde product was observed. Selective functionalization of the tertiary C—H bond was observed, supporting our hypotheses of reactivity in these reactions. Application of this protocol in the functionalization of substituted aryl and alkyl aldehydes is currently under development as a part of our efforts to establish the substrate scope of this reaction. Since, the allyl transfer reaction of



Scheme 11. Attempted allyl transfer reaction of *N*,*N*-dimethylaniline with **3**.



Scheme 12. Predicted pathway for dimerization of *N*,*N*-dimethylaniline.

N,*N*-dimethylaniline yielded the unexpected dimerized product **51**, we envisioned that the non-aromatic amines would be a better choice for functionalization of amines via allyl transfer reaction.

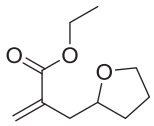
4. Experimental

4.1. General procedure for allyl transfer reaction of ethers

Allyl transfer reactions of ethers were run in 20 mL Pyrex pressure tubes. In a 20 mL Pyrex tube, allyl-PINO substrate (**3** or **4**, 0.00090 mol) was mixed with the desired ether substrate (approx. 2—3 mL). Initiator, di-*tert*-butyl peroxide (0.000136 mol) was added to the above mixture. This reaction mixture was degassed using high vacuum by freeze-pump-thaw (3X) method and it was heated at 120 °C while stirring. The temperature fluctuation was ±5 °C and the time of the reaction run has the accuracy of ±1 min. At the end of each reaction, the pressure tube was cooled under tap water followed by solvent evaporation (if necessary) or liquid-liquid extraction to yield the crude product. The crude product was then

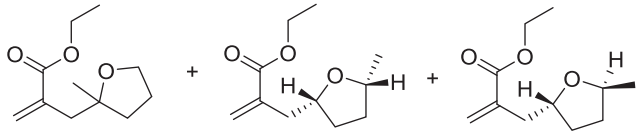
purified using flash chromatography (20% ethyl acetate: 80% hexanes). Reaction yields were determined by GC using diphenylmethane as an internal standard.

4.2. Experimental data



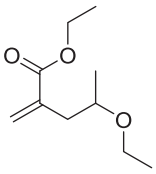
9

*4.2.1. Ethyl 2-((tetrahydrofuran-2-yl)methyl)acrylate (**9**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.23 (1 H, d, *J* 1.3), 5.66 (1 H, d, *J* 1.2), 4.21 (2 H, q, *J* 7.1), 4.08–3.99 (1 H, m), 3.91–3.83 (1 H, m), 3.77–3.68 (1 H, m), 2.52 (2 H, d, *J* 6.4), 2.06–1.79 (3 H, m), 1.59–1.44 (2 H, m), 1.30 (3 H, t, *J* 7.1). **^{13}C NMR** (101 MHz, $CDCl_3$) 167.31, 137.78, 126.19, 100.56, 67.20, 60.45, 37.66, 32.18, 24.18, 14.21. **HRMS**: Calculated for $C_{10}H_{16}O_3$ 185.1172, observed [M+H] 185.1180 (+4.41 ppm).



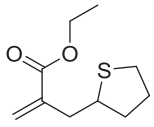
25 27

*4.2.2. Ethyl 2-((2-methyltetrahydrofuran-2-yl)methyl)acrylate (**25**)+ mixture of **27**.* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.19 (1 H, d, *J* 1.8), 5.60–5.59 (1 H, m), 4.25–4.15 (3 H, m), 3.80 (2 H, dd, *J* 14.7, 6.8), 2.55 (3 H, q, *J* 13.5), 1.98–1.86 (2 H, m), 1.84–1.74 (1 H, m), 1.68–1.57 (2 H, m), 1.29 (4 H, td, *J* 7.1, 1.6), 1.18 (3 H, s). (Expansion in the 1.31–1.39 region shows evidence of regioisomers (cis and trans **27**) in the form of 3H, d). **^{13}C NMR** (101 MHz, $CDCl_3$) 168.25, 137.47, 127.52, 81.92, 67.51, 60.77, 41.49, 36.72, 25.75, 21.28, 14.23. **HRMS**: Calculated for $C_{11}H_{18}O_3$ (3–95) 199.1329, observed [M+H] 199.1325 (−2.06 ppm).



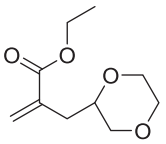
5

*4.2.3. Ethyl 4-ethoxy-2-methylenepentanoate (**5**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.11 (1 H, dd, *J* 4.1, 1.9), 5.52 (1 H, dq, *J* 1.7, 1.2), 4.12 (2 H, q), 3.45–3.33 (2 H, m), 2.51 (1 H, ddd, *J* 13.8, 6.6, 1.0), 2.27 (1 H, ddd, *J* 13.8, 6.1, 1.0), 1.22 (3 H, td, *J* 7.1, 2.4), 1.11–1.03 (5 H, m). **^{13}C NMR** (101 MHz, $CDCl_3$) 167.16, 137.72, 126.80, 73.63, 63.51, 60.34, 39.27, 19.44, 15.57, 13.97. **HRMS**: Calculated for $C_{10}H_{18}O_3$ 187.1329, observed [M+H] 187.1325 (−1.82 ppm).



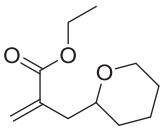
15

*4.2.4. Ethyl 2-((tetrahydrothiophen-2-yl)methyl)acrylate (**15**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.25–6.12 (1 H, m), 5.61 (1 H, q, *J* 1.2), 4.20 (2 H, q, *J* 7.2), 3.66–3.49 (1 H, m), 3.29–3.19 (1 H, m), 2.00 (8 H, dddd, *J* 178.1, 129.7, 63.6, 6.9), 1.29 (3 H, t, *J* 7.1). **^{13}C NMR** (101 MHz, $CDCl_3$) 166.92, 139.20, 125.84, 60.40, 46.98, 39.58, 36.95, 32.17, 30.00, 14.48. **HRMS**: Calculated for $C_{10}H_{16}O_2S$ 201.0944, observed [M+H] 201.0946 (+1.27).



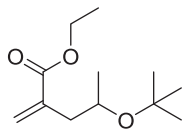
13

*4.2.5. Ethyl 2-((1,4-dioxan-2-yl)methyl)acrylate (**13**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.24 (1 H, d, *J* 1.4), 5.65 (1 H, q, *J* 1.2), 4.21 (2 H, q, *J* 7.1), 3.82–3.50 (6 H, m), 2.42–2.38 (2 H, m), 1.30 (3 H, t, *J* 7.1). **^{13}C NMR** (101 MHz, $CDCl_3$) 166.64, 136.00, 127.44, 73.57, 71.04, 66.88, 66.20, 60.92, 34.21, 14.37. **HRMS**: Calculated for $C_{10}H_{16}O_4$ 201.1121, observed [M+H] 201.1127 (+2.78).



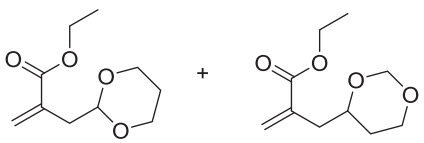
11

*4.2.6. Ethyl 2-((tetrahydro-2H-pyran-2-yl)methyl)acrylate (**11**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.20 (1 H, d, *J* 1.7), 5.62 (1 H, dd, *J* 2.7, 1.3), 4.20 (2 H, q, *J* 7.2), 4.00–3.90 (1 H, m), 3.53–3.32 (2 H, m), 2.52–2.36 (2 H, m), 1.90–1.35 (7 H, m), 1.29 (3 H, t, *J* 7.1). **^{13}C NMR** (101 MHz, $CDCl_3$) 167.32, 137.51, 126.90, 76.10, 68.72, 60.58, 39.13, 31.79, 25.93, 23.34, 14.26. **HRMS**: Calculated for $C_{11}H_{18}O_3$ 199.1329, observed [M+H] 199.1322 (−3.17 ppm).



6

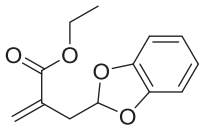
*4.2.7. Ethyl 4-(tert-butoxy)-2-methylenepentanoate (**6**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.17 (1 H, q), 5.57 (1 H, s), 4.22 (2 H, q), 3.87–3.78 (1 H, m), 2.48 (1 H, dd), 2.34 (1 H, dd), 1.30 (5 H, t), 1.16 (11 H, s), 1.09 (4 H, d). **^{13}C NMR** (101 MHz, $CDCl_3$) 167.38, 138.54, 127.04, 73.35, 65.86, 60.48, 42.02, 28.61, 22.55, 14.09. **HRMS**: Calculated for $C_{12}H_{22}O_3$ 215.1642, observed [M+H] 215.1626 (−7.36).



30 32

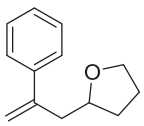
*4.2.8. Ethyl 2-((1,3-dioxan-2-yl)methyl)acrylate (**30**+**32**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.24 (2 H, dd, *J* 3.8, 1.5), 5.68 (2 H, dd, *J* 3.1, 1.2), 4.74 (1 H, t), 4.21 (3 H, q, *J* 7.1), 4.08 (3 H, dd, *J* 6.0, 4.7), 4.05–3.98 (1 H, m), 3.88–3.58 (4 H, m), 2.62 (3 H, dd, *J* 5.4, 0.9), 2.24–1.96 (2 H, m), 1.30 (10 H, s). **^{13}C NMR** (101 MHz, $CDCl_3$) 177.89, 135.50, 128.46,

123.37, 67.19, 60.15, 37.66, 25.44, 13.61. **HRMS**: Calculated for $C_{10}H_{16}O_4$ 201.1112, observed 201.110 (+2.17 ppm).



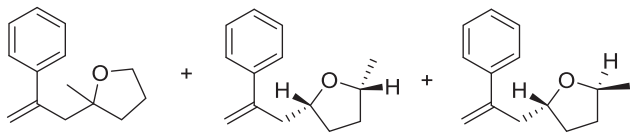
17

*4.2.9. Ethyl 2-(benzo[1,3]dioxol-2-ylmethyl)acrylate (**17**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 6.89–6.69 (2 H, m), 6.37 (1 H, d, *J* 1.2), 6.31 (1 H, t, *J* 5.1), 5.80 (1 H, q, *J* 1.2), 4.25 (1 H, q, *J* 7.1), 3.03–2.88 (1 H, m), 1.32 (1 H, t, *J* 7.1). **^{13}C NMR** (101 MHz, $CDCl_3$) 166.29, 147.09, 133.94, 129.08, 121.71, 109.50, 108.87, 60.77, 37.35, 13.92. **HRMS**: Calculated for $C_{13}H_{14}O_4$ 235.0965, observed [M+H] 235.0975 (+4.5 ppm).



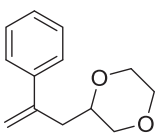
10

*4.2.10. 2-(2-Phenylallyl)tetrahydrofuran (**10**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.49–7.23 (4 H, m), 5.36 (1 H, d, *J* 1.3), 5.18 (1 H, d, *J* 1.2), 3.99–3.86 (1 H, m), 3.75–3.67 (1 H, m), 2.91 (1 H, ddd, *J* 14.3, 6.4, 1.1), 2.62 (1 H, ddd, *J* 14.3, 6.9, 0.9), 1.98–1.75 (3 H, m), 1.53 (1 H, td, *J* 7.5, 3.0). **^{13}C NMR** (101 MHz, $CDCl_3$) 145.49, 141.22, 128.39, 127.61, 126.19, 114.41, 77.54, 67.80, 41.58, 31.14, 25.54. **HRMS**: Calculated for $C_{13}H_{16}O$ 189.1274, observed [M+H] 189.1259 (−7.71 ppm).



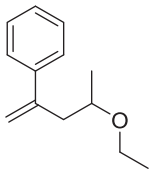
26 28

*4.2.11. 2-Methyl-2-(2-phenylallyl)tetrahydrofuran (**26**+**28**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.36 (2 H, d, *J* 50.6), 5.34 (1 H, s), 5.17 (1 H, s), 3.75 (1 H, ddt, *J* 21.9, 8.2, 6.8), 2.78 (1 H, s), 1.85 (2 H, s), 1.12 (1 H, s). **^{13}C NMR** (101 MHz, $CDCl_3$) 146.08, 142.87, 128.13, 127.10, 126.50, 116.93, 82.81, 66.83, 46.07, 36.03, 26.36, 25.94. **HRMS**: Calculated for $C_{14}H_{18}O$ 203.143, observed [M+H] 203.1414 (−7.86 ppm).



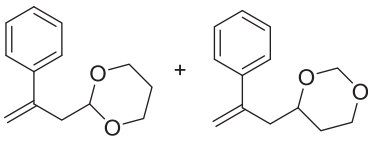
14

*4.2.12. 2-(2-Phenylallyl)-1,4-dioxane (**14**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.50–7.15 (4 H, m), 5.36 (1 H, d, *J* 1.4), 5.15 (1 H, q, *J* 1.2), 3.86–3.46 (5 H, m), 3.29 (1 H, dd, *J* 11.4, 9.8), 2.76 (1 H, ddd, *J* 14.4, 6.5, 1.2), 2.52 (1 H, ddd, *J* 14.5, 7.0, 1.0). **^{13}C NMR** (101 MHz, $CDCl_3$) 143.89, 140.37, 128.40, 127.65, 126.15, 115.01, 73.53, 71.05, 66.86, 66.39, 38.16. **HRMS**: Calculated for $C_{13}H_{16}O_2$ 205.1225, observed [M+H] 205.1229 (+0.87 ppm).



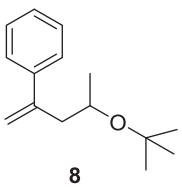
7

*4.2.13. (4-Ethoxypent-1-en-2-yl)benzene (**7**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.49–7.17 (1 H, m), 5.32 (1 H, d, *J* 1.6), 5.14 (1 H, d, *J* 1.3), 3.64–3.26 (1 H, m), 2.93 (1 H, ddd, *J* 14.0, 6.0, 1.1), 2.50 (1 H, ddd, *J* 14.0, 7.3, 1.0), 1.14 (1 H, t, *J* 6.9). **^{13}C NMR** (101 MHz, $CDCl_3$) 145.92, 141.39, 128.27, 127.19, 126.35, 114.68, 73.73, 63.67, 42.75, 19.51, 15.57. **HRMS**: Calculated for $C_{13}H_{18}O$ 191.143, observed [M+H] 191.1427 (−1.72 ppm).



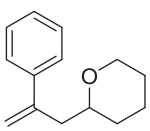
29 31

*4.2.14. 2-(2-Phenylallyl)-1,3-dioxane (**29**) (major 60%) and 4-(2-phenylallyl)-1,3-dioxane (**31**) (minor 40%).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.61–7.04 (5 H, m), 5.39 (1 H, dd, *J* 9.5, 1.4), 5.19 (1 H, dq, *J* 12.3, 1.3), 4.68–4.52 (1 H, m), 4.15–3.99 (1 H, m), 3.80–3.50 (2 H, m), 2.84 (1 H, dd, *J* 5.3, 1.1), 2.08 (1 H, ddd, *J* 13.4, 13.0, 10.0). **^{13}C NMR** (101 MHz, $CDCl_3$) 144.30, 143.01, 140.81, 140.64, 128.41, 128.29, 127.60, 127.46, 126.17, 126.15, 115.21, 100.69, 93.47, 74.82, 67.20, 66.51, 42.01, 41.08, 31.62, 25.86. **HRMS**: Calculated for C_{13} H_{16} O_2 205.1223, observed [M+H] 205.1225 (+0.89 ppm).



8

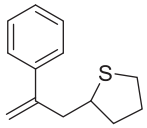
*4.2.15. (4-(tert-Butoxy)pent-1-en-2-yl)benzene (**8**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.54–7.20 (1 H, m), 5.32 (1 H, d, *J* 1.7), 5.13 (1 H, dd, *J* 2.2, 1.4), 3.78–3.50 (1 H, m), 2.85 (1 H, ddd, *J* 13.8, 5.5, 1.0), 2.52 (1 H, ddd, *J* 13.8, 8.1, 0.7), 1.22–1.03 (2 H, m). **^{13}C NMR** (101 MHz, $CDCl_3$) 146.12, 141.09, 128.41, 127.40, 126.31, 114.74, 73.41, 66.21, 45.41, 28.52, 22.64. **HMRS**: Difficult to ionize using ESI or APCI ionization methods (GC–MS analysis can be found in Supplementary data S6, Fig. S11.).



12

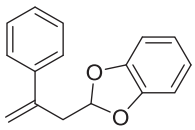
*4.2.16. 2-(2-Phenylallyl)tetrahydro-2H-pyran (**12**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.47–7.38 (2 H, m), 7.31 (3 H, dddd, *J* 13.1, 11.6, 5.8, 3.6), 5.34 (1 H, d, *J* 1.6), 5.14 (1 H, dd, *J* 2.6, 1.3), 4.03–3.89 (1 H, m), 3.47–3.24 (2 H, m), 2.83 (1 H, ddd, *J* 14.3, 6.5, 1.1), 2.55 (1 H, ddd, *J* 14.3, 6.7, 1.0),

1.88–1.16 (7 H, m). **^{13}C NMR** (101 MHz, $CDCl_3$) 145.14, 140.98, 128.45, 127.20, 126.18, 75.94, 68.53, 42.76, 31.85, 26.14, 23.24. **HMRS**: Calculated for $C_{14}H_{18}O$ 203.143, observed [M+H] 203.1436 (+2.54 ppm).



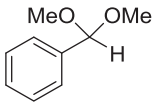
16

*4.2.17. 2-(2-Phenylallyl)tetrahydrothiophene (**16**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.47–7.07 (5 H, m), 5.32–5.24 (1 H, m), 5.17–5.04 (1 H, m), 2.90–2.68 (10 H, m), 1.96–1.83 (8 H, m), 1.26 (7 H, s), 0.87 (6 H, s). **^{13}C NMR** (101 MHz, $CDCl_3$) 147.09, 140.87, 128.28, 127.45, 126.20, 113.83, 36.73, 31.74, 30.93, 22.64, 14.17. **HRMS**: Calculated for C_{13} H_{16} S: 205.1045, observed [M+H] 205.1052 (+3.27 ppm).



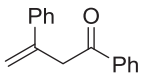
18

*4.2.18. 2-(2-Phenylallyl)benzo[1,3]dioxole (**18**).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.56–7.21 (2 H, m), 6.93–6.71 (6 H, m), 6.23 (1 H, t, *J* 5.1), 6.00–5.87 (3 H, m), 5.52 (1 H, d, *J* 1.1), 5.32 (1 H, d, *J* 1.1), 3.16 (1 H, dd, *J* 5.1, 1.0). **^{13}C NMR** (101 MHz, $CDCl_3$) 147.50, 141.36, 140.35, 128.30, 127.88, 126.32, 121.72, 116.23, 108.88, 100.36, 40.58. **HMRS**: Calculated for $C_{16}H_{12}O_2$ 237.0910, observed [M+H] 237.0927 (+7.1).



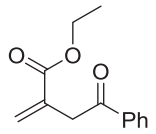
43

*4.2.19. (Dimethoxymethyl)benzene (**43**).* Based on a literature procedure.[20] A mixture of benzaldehyde (2 g, 0.01886 mol), $CoCl_2$ (dry, 0.121 g, 0.000943 mol) and dry methanol (80 mL) were refluxed at 110 °C for 3 h, using $CaCl_2$ guard tube over reflux condenser. Methanol was evaporated under reduced pressure. Ethyl acetate (5 mL) was added to the residue. Co(II) salt was filtered and filtrate was passed through a short column of alumina (basic) using 5% ethyl acetate in hexane. Procedure yielded pure dimethyl acetal product which was characterized by NMR. **^{1}H NMR** (400 MHz, $CDCl_3$) 7.50–7.30 (4 H, m), 5.41 (1 H, s), 3.34 (6 H, s). **^{13}C NMR** (101 MHz, $CDCl_3$) 138.20, 128.53, 128.07, 126.63, 103.25, 52.76.



45 (Z=Ph)

*4.2.20. 1,3-Diphenylbut-3-en-1-one (**45**, Z=Ph).* **^{1}H NMR** (400 MHz, $CDCl_3$) 8.00–6.76 (1 H, m), 5.49 (1 H, dd, *J* 1.3, 0.5), 5.02 (1 H, q, *J* 1.3), 3.84 (1 H, s). **^{13}C NMR** (101 MHz, $CDCl_3$) 193.54, 147.25, 139.50, 129.04, 128.45, 128.35, 127.57, 126.26, 114.82, 41.96. **HRMS**: Calculated for $C_{16}H_{14}O$, 223.2811, observed 223. 1112 (+5.69 ppm).



45 Z=CO_2Et

*4.2.21. Ethyl 2-methylene-4-oxo-4-phenylbutanoate (**45**, Z=CO_2Et).* **^{1}H NMR** (400 MHz, $CDCl_3$) 7.99 (2 H, ddd, *J* 7.1, 2.3, 1.2), 7.65–7.41 (4 H, m), 6.44–6.36 (1 H, m), 5.69 (1 H, q, *J* 1.0), 4.21 (2 H, q, *J* 7.2), 4.00 (2 H, d, *J* 1.0), 1.26 (4 H, t, *J* 7.1). **^{13}C NMR** (101 MHz, $CDCl_3$) 196.76, 166.29, 134.82, 133.25, 128.62, 128.30, 128.23, 61.08, 41.81, 13.93. **HRMS**: Calculated for $C_{13}H_{15}O_3$ 219.1016, observed 219.101 (−2.63).

Acknowledgements

Acknowledgment is made to the donors of American Chemical Society, Petroleum Research Fund for the support of this project. The authors also wish to thank Mr. Mehdi Ashraf-Khorassani for his help with HRMS and ESI-MS analyses, and Mr. Justin Curtiss for synthetic assistance.

Supplementary data

Supplementary data (Supplementary data for procedures of synthetic reactions, ^{1}H and ^{13}C NMR spectral data, HRMS data, kinetic chain length calculations, and GC–MS analyses of regioisomeric products) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2016.05.046.

References and notes

1. *Frontmatter. In Handbook of C–H Transformations*; Dyker, G., Ed.; Wiley-VCH Verlag GmbH: 2008; pp I–XXVI.
2. (a) Chen, C.; Crich, D.; Papadatos, A. *J. Am. Chem. Soc.* **1992**, *114*, 8313–8314; (b) Muramatsu, H.; Moriguchi, S.; Inukai, K. *J. Org. Chem.* **1966**, *31*, 1306–1309.
3. (a) Davies, H. M. L.; Hansen, T. *J. Am. Chem. Soc.* **1997**, *119*, 9075–9076; (b) Davies, H. M. L.; Yang, J.; Nikolai, J. *J. Organomet. Chem.* **2005**, *690*, 6111–6124; (c) Davies, H. M. L.; Grazini, M. V. A.; Aouad, E. *Org. Lett.* **2001**, *3*, 1475–1477; (d) Davies, H. M. L.; Manning, J. R. *Nature* **2008** 451–417; (e) Davies, H. M. L.; Beckwith, R. E. J.; Antoulinakis, E. G.; Jin, Q. *J. Org. Chem.* **2003**, *68*, 6126–6132; (f) Davies, H. M. L.; Hedley, S. J.; Bohall, B. R. *J. Org. Chem.* **2005**, *70*, 10737–10742; (g) Davies, H. M. L.; Hansen, T.; Churchill, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 3063–3070; (h) Díaz-Requejo, M. M.; Belderraín, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 896–897.
4. (a) Perez, D.; Leighton, F.; Aspee, A.; Aliaga, C.; Lissi, E. *Biol. Res.* **2000**, *33*; (b) Wang, P.; Adams, J. *J. Am. Chem. Soc.* **1994**, *116*, 3296–3305.
5. (a) Muramatsu, H.; Inukai, K.; Ueda, T. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 903–907; (b) Chambers, R. D.; Fuss, R. W.; Jones, M. *J. Fluorine Chem.* **1990**, *49*, 409–419; (c) Chen, J.; Krichmeier, R. L.; Shreeve, J. M. *Inorg. Chem.* **1996**, *35*, 6676–6681.
6. (a) Gong, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 4486–4487; (b) Xiang, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 11986–11987; (c) Xiang, J.; Jiang, W.; Gong, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1997**, *119*, 4123–4129; (d) Alkema, H. J.; Arens, J. F., Chemistry of acetylenic ethers XLVI Addition of thiols to acetylenic ethers. **1960**, *79*, 1257–1281.
7. Hirano, K.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2002**, *43*, 3617–3620.
8. Liu, Z.-Q.; Sun, L.; Wang, J.-G.; Han, J.; Zhao, Y.-K.; Zhou, B. *Org. Lett.* **2009**, *11*, 1437–1439.
9. (a) Yamamoto, Y.; Yamada, K.-I.; Tomioka, K. *Tetrahedron Lett.* **2004**, *45*, 795–797; (b) Yamada, K. I.; Yamamoto, Y.; Tomioka, K. *Org. Lett.* **2003**, *5*, 1797–1799; (c) Yamada, K. i; Yamamoto, Y.; Maekawa, M.; Tomioka, K. *J. Org. Chem.* **2004**, *69*, 1531–1534; (d) Yamamoto, Y.; Maekawa, M.; Akindele, T.; Yamada, K.-I.; Tomioka, K. *Tetrahedron Lett.* **2005**, *61*, 379–384; (e) Clerici, A.; Cannella, R.; Pastori, N.; Panzeri, W.; Porta, O. *Tetrahedron Lett.* **2006**, *62*, 5986–5994.
10. (a) Tanko, J. M.; Sadeghipour, M. *Angew. Chem.* **1999**, *111*, 219–222; (b) Struss, J. A.; Mitra, S.; Tanko, J. M. *Tetrahedron Lett.* **2009**, *50*, 2119–2120; (c) Patil, S.; Chen, L.; Tanko, J. M. *Eur. J. Org. Chem.* **2014**, *2014*, 502–505; (d) Patil, S.; Chen, L.; Tanko, J. M. *Tetrahedron Lett.* **2014**, *55*, 7029–7033.

11. Mayo, F. R. Free Radicals In*Kochi, Jay K., Ed.Vol. II; Wiley: New York, NY, 1973; Vol. II, p 906; J. Poly. Sci.: Poly. Lett. Ed.* ***1974****, 12 (9), 536–538.*
12. Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255–263.
13. Koshino, N.; Saha, B.; Espenson, J. H. *J.Org. Chem.* **2003**, *68*, 9364–9370.
14. (a) Jaenicke, L. Ionophore Polyether Antibiotics – Naturally Occurring Acid Ionophores. Bd. 1: Biology In*Westley, Von J. W., Ed.XVII, 465 S., SFr; Marcel Dekker: New York – Basel, 1982; XVII, 465 S., SFr, p 185; Nachrichten aus Chemie, Technik und Laboratorium* ***1983****, 31 (9), 724–724; (b) Alali, F. Q.; Liu, X.-X.; McLaughlin, J. L. J. Nat. Prod.* **1999**, *62*, 504–540; (c) Harmange, J.-C.; Figadère, B. *Tetrahedron: Asymmetry* **1993**, *4*, 1711–1754.
15. (a) Wolfe, J. P.; Rossi, M. A. *J. Am. Chem. Soc.* **2004**, *126*, 1620–1621; (b) Qian, H.; Han, X.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 9536–9537; (c) Sromek, A. W.; Kel'in, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 2280–2282; (d) Antoniotti, S.; Genin, E.; Michelet, V.; Genêt, J.-P. *J. Am. Chem. Soc.* **2005**, *127*, 9976–9977.
16. Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*; McGraw-Hill: New York, NY, 1995.
17. Velusamy, S.; Punniyamurthy, T. *Tetrahedron Lett.* **2004**, *45*, 4917–4920.
18. Luo, Y.-R. Tabulated BDEs of C–H Bonds In *Handbook of Bond Dissociation Energies in Organic Compounds*; CRC Press: 2002.
19. Baciocchi, E.; Bietti, M.; Gerini, M. F.; Lanzalunga, O. *J. Org. Chem.* **2005**, *70*, 5144–5149.
20. Punniyamurthy, T.; Velusamy, S.; Iqbal, J. *Chem. Rev.* **2005**, *105*, 2329–2364.

Please cite this article in press as: Patil, S. V.; Tanko, J. M., Tetrahedron (2016), http://dx.doi.org/10.1016/j.tet.2016.05.046