Tetrahedron Letters 51 (2010) 4452–4454

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Unprecedented copper(I)-catalyzed photochemical reaction of diethyl ether with vicinal diols and ketals

Sujit Mondal, Ram Naresh Yadav, Subrata Ghosh *

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700 032, India

A R T I C L E I N F O

Article history:
Received 31 May 2010
Revised 15 June 2010
Accepted 17 June 2010
Available online 20 June 2010

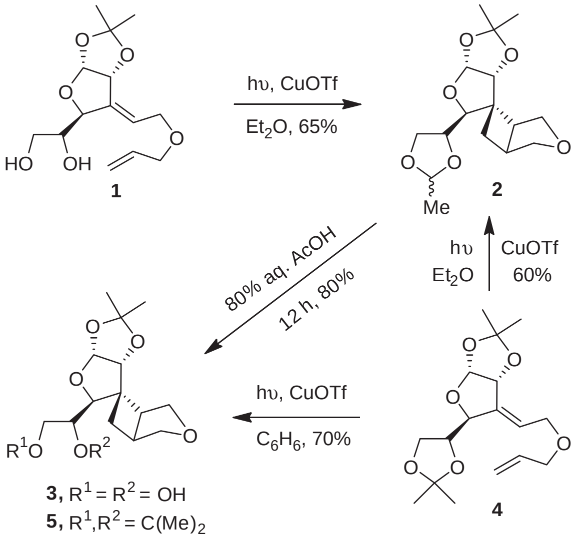
Keywords:
Acetals
Photochemistry
Catalysis

ABSTRACT

A novel Cu(I)-catalyzed photochemical reaction of diethyl ether with vicinal diols and their ketals is reported. The most remarkable feature is the transformation of 1,2-diols and their ketals to acetals of acetaldehyde under totally neutral condition without using acetaldehyde.

Photochemical reactions[1] offer a wide range of fascinating and useful transformations in organic chemistry that are generally not observed in ground state reactions. Photochemistry of compounds such as alkenes, acyclic and cyclic dienes, ketones, unsaturated ketones, and aromatic compounds having a plethora of functional groups has been investigated in detail. Of these, [2+2] cycloaddition[2,3] of alkenes to form cyclobutanes is one of the most widely studied synthetically valuable photochemical reactions. Metal catalysts[3] have profound influence on the course of photochemical reactions. For example, unlike the facile photoaddition of enones to alkenes, simple alkenes do not add to each other under direct or sensitized irradiation. However, addition of simple alkenes can be achieved efficiently in metal-catalyzed photochemical reactions. Of the various metal salts investigated, copper(I) salts especially copper(I) triflate have been found to be very efficient in accomplishing [2+2] photocycloaddition of simple alkenes.[3,4] This process finds extensive applications in synthetic organic chemistry.[5,6] Herein, we report a new copper(I)-catalyzed photochemical reaction in which vicinal diols and ketals are transformed to acetals of acetaldehyde on reaction with diethyl ether.

As part of our continued interest[7] in the applications of copper(I)-catalyzed [2+2] photocycloaddition reaction in natural products synthesis, we required an intramolecular photocycloaddition of the diene **1** as the key step (Scheme 1). Generally copper(I) triflate-catalyzed photochemical reactions are carried out in diethyl ether as solvent. Thus a solution of the diene **1** in diethyl ether was irradiated[7] in the presence of $(CuOTf)_2 \cdot C_6H_6$ complex (15–20 mol %) in Ar atmosphere. To our surprise the cyclobutane derivative **2** was obtained as a diastereoisomeric mixture in 65% yield[8] instead of the desired cyclobutane derivative **3**. More surprisingly, when the ketal **4** was irradiated in diethyl ether under identical conditions the same cyclobutane derivative **2** was obtained in 60% yield. Treatment of the acetal **2** with aqueous acetic acid led to the diol **3** as a single diastereoisomer indicating that cycloaddition took place in a stereocontrolled manner.



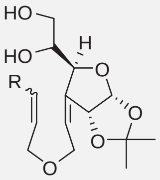
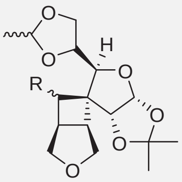
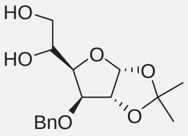
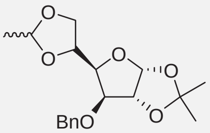
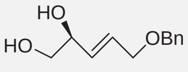
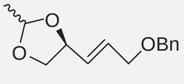
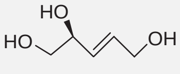
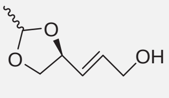
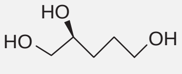
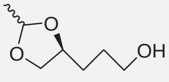
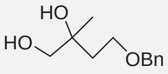
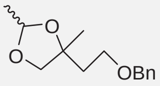
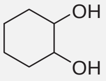
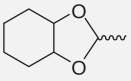
Scheme 1. Cu(I)-catalyzed photochemical reaction of diene–diol in diethyl ether.

---

* Corresponding author. Tel.: +91 33 2473 4971; fax: +91 33 2473 2805.
E-mail address: ocsg@iacs.res.in (S. Ghosh).

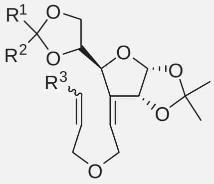
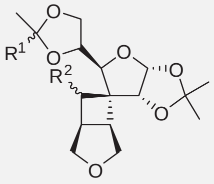
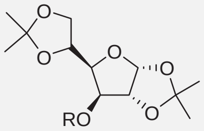
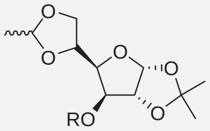
0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.06.080

Table 1
Cu(I)-catalyzed photochemical reaction of vicinal diols with diethyl ether[a]

Entry	Substrate	Product[b]	Yield[c] (%)
			
1	**1**, R = H	**2**, R = H	65
2	**6**, R = CH_2:CHMe	**7**, R = CH_2:CHMe	60
3	 **8**	 **9**	70
4	 **10**	 **11**	60
5	 **12**	 **13**	70
6	 **14**	 **15**	65
7	 **16**	 **17**	55
8	 **18**	 **19**	68

[a] Reactions were complete in 4–6 h.
[b] All products were obtained as a mixture of diastereomers.
[c] Yields refer to chromatographically isolated pure products.

Table 2
Cu(I)-catalyzed photochemical reaction of ketals with diethyl ether[a]

Entry	Substrate	Product[b]	Yield[c] (%)
			
1	**4**, $R^1 = R^2$ = Me, R^3 = H	**2**, $R^1 = R^2$ = H	65
2	**20**, $R^1 = R^2 = R^3$ = Me	**21**, R^1 = H, R^2 = Me	60
3	**22**, $R^1,R^2 = -(CH_2)_5-$, R^3 = H	**2**	65
			
4	**23**, R = Bn	**9**, R = Bn	65
5	**24**, R = H	**25**, R = H	60

[a] Reactions were complete in 3–4 h.
[b] Products were obtained as diastereomeric mixture.
[c] Yields refer to chromatographically isolated pure products.

Addition reactions to the sp^2 center at C-3 of diacetone glucose[9] derivatives generally take place from the face opposite to the 1,2-acetonide moiety. Based on this reactivity trend the structure of the cyclobutane derivative obtained from cycloaddition of the dienes **1** and **4** was assigned the structure **2**.

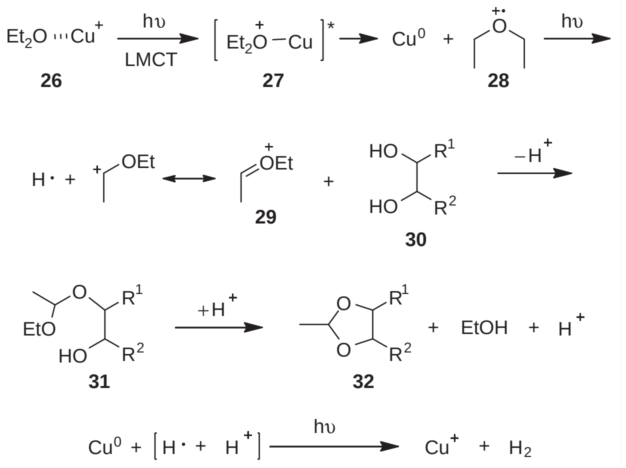
Transformation of the dienes **1** and **4** to the same adduct **2** involves, in addition to [2+2] cycloaddition, protection of the vicinal diol unit as acetaldehyde acetal in case of **1** and chemoselective transformation of the more labile 5,6-acetonide moiety to the acetal in case of **4**. Both these transformations generally require acetaldehyde or its dimethyl acetal and an acid as catalyst.[10] These transformations accomplished under totally neutral condition without using any carbonyl compound are spectacular.

To explore the generality of these novel transformations, a number of vicinal diols and acetonides were subjected to irradiation under copper(I) catalysis and the results are summarized in Tables 1 and 2, respectively. It may be noted while the diol–dienes **1** and **6** (Table 1, entries 1 and 2) underwent cycloaddition with concomitant protection of the diol unit, the vicinal diols **8**, **10**, **12**, **14**, **16**, and **18** (Table 1, entries 3–8) lacking diene units were protected to give acetals **9**, **11**, **13**, **15**, **17**, and **19**, respectively in very good yields.

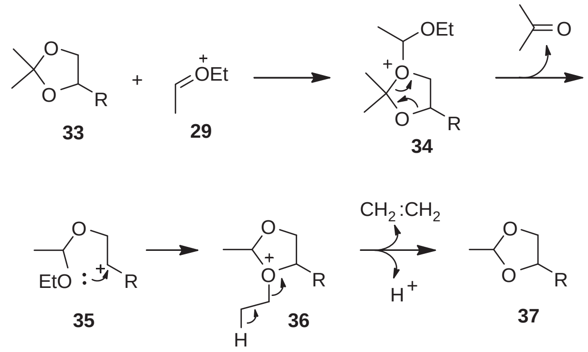
Similarly, the acetonide derivatives **4**, **20**, and **22** (Table 2, entries 1–3) underwent *trans*-acetalization with simultaneous cycloaddition to afford adducts **2**, **21**, and **2**, respectively. The acetonide derivatives **23** and **24** (Table 2, entries 4 and 5) lacking any alkene unit also underwent *trans*-acetalization to produce the acetals **9** and **25**, respectively.

In order to explore the course of these novel transformations, irradiation of **4** was carried out in benzene. Cycloaddition took place as expected but amazingly the acetonide unit remained unchanged to afford the adduct **5** in 70% yield. This clearly indicated the participation of diethyl ether in the protection of the vicinal diol unit to the acetal of acetaldehyde. Further, the necessity of copper(I) catalyst in accomplishing these photo-induced transformations was established from the failure of **24** to provide **25** in the absence of CuOTf. To the best of our knowledge there are very few reports on the photochemical reaction of diethyl ether.[11]

A possible mechanism for these transformations is depicted in Scheme 2. Copper(I)-catalyzed photochemical reactions are believed to proceed through formation of a ground state Cu(I) complex in which alkene as well as hydroxy/alkoxy group acts as ligand. Thus coordination of diethyl ether with Cu(I) leads to the complex **26**. Photoactivation of this complex initiates ligand (O) to metal (Cu^+) charge transfer (LMCT)[12] to generate **27**. The latter



Scheme 2. A plausible reaction course.



Scheme 3. Probable mechanism for *trans*-acetalization.

leads to the radical cation **28** which is then transformed to the activated acetaldehyde equivalent **29** on loss of one H radical.[13] Acetalization of the diol **30** with **29** proceeds in the usual way to produce the acetal **32** through protonation of **31**. Oxidation of Cu(0) regenerates the catalyst Cu^+ with evolution of H_2.[3]

Probably, a sequence (Scheme 3) similar to the one described in Scheme 2 is responsible for *trans*-acetalization of the acetonides. This is accompanied by the expulsion of acetone and ethylene. Indeed, when the cyclohexylidine derivative **22** was subjected to the above-mentioned reaction condition cyclohexanone was isolated in quantitative yield. Regeneration of Cu^+ catalyst takes place in the same way as depicted in Scheme 2.

In conclusion, a new Cu(I)-catalyzed photochemical reaction of diethyl ether with vicinal diols has been discovered. The most remarkable feature is the transformation of 1,2-diols and their ketals to acetals of acetaldehyde under totally neutral condition without using acetaldehyde. It may be noted that acetals can be cleaved photochemically[14] to regenerate diols and aldehydes. However, to the best of our knowledge there is no report on protection of diols to acetals under photochemical conditions. The present technique eliminates the disadvantages of employing acetaldehyde for protection of diols under acid catalysis.

Acknowledgments

Financial support from the Department of Science and Technology, Govt. of India, through Ramanna Fellowship to S.G. is gratefully acknowledged. S.M. and R.N.Y. thank CSIR, New Delhi, for Senior Research Fellowships.

References and notes

1. Reviews on general photochemical reactions and its use in natural product synthesis see: (a) Horspool, W. M. *Synthetic Organic Photochemistry*; Plenum Press: New York-London, 1984; (b) Coyle, J. D. *Photochemistry in Organic Synthesis*; Royal Society of Chemistry: London, 1986; (c) Crimmins, M. T.; Porco, J. A.; Schreiber, S. L.; Lucchi, O. D.; Adam, W.; Demuth, M. I.. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, pp 123–215; (d) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741; (e) Zhang, M.; Lu, Z.-F.; Liu, Y.; Grampp, G.; Hu, H.-W.; Xu, J.-H. *Tetrahedron* **2006**, *62*, 5663; (f) Liu, R. S. H.; Hammond, G. S. *Acc. Chem. Res.* **2005**, *38*, 396; (g) Griesbeck, A. G.; Hoffmann, N.; Warzecha, K.-D. *Acc. Chem. Res.* **2007**, *40*, 128; (h) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052; (i) Kohmoto, S.; Hisamatsu, S.; Mitsuhashi, H.; Takahashi, M.; Masu, H.; Azumaya, I.; Yamaguchi, K.; Kishikawa, K. *Org. Biomol. Chem.* **2010**, *8*, 2174. and references cited therein.
2. For reviews on [2+2] photocycloaddition reactions see: (a) Crimmins, M. T. *Chem. Rev.* **1988**, *88*, 1453; (b) Dekeukeleire, D.; He, S. H. *Chem. Rev.* **1993**, *93*, ; 359; (c) Winkler, J. D.; Mazur-Bowen, C.; Liotta, F. *Chem. Rev.* **1995**, *95*, 2003; (d) Bach, T. *Synthesis* **1998**, 683; (e) Namyslo, J. C.; Kaufmann, D. E. *Chem. Rev.* **2003**, *103*, 1485; Selected recent works: (f) Crimmins, M. T.; Wang, Z.; Mckerlie, L. A. *J. Am. Chem. Soc.* **1998**, *120*, 1747; (g) Bach, T.; Bergmann, H. *J. Am. Chem. Soc.* **2000**, *122*, 11525; (h) Selig, P.; Bach, T. *J. Org. Chem.* **2006**, *71*, 5662; (i) Iriondo-Alberdi, J.; Greaney, M. F. *Eur. J. Org. Chem.* **2007**, 4801; (j) Albrecht, D.; Basler, B.; Bach, T. *J. Org. Chem.* **2008**, *73*, 2345; (k) Albrecht, D.; Vogt, F.; Bach, T. *Chem. Eur. J.* **2010**, *16*, 4284. and references cited therein.
3. For review on metal-catalyzed photochemical reactions, see: Salomon, R. G. *Tetrahedron* **1983**, *39*, 485.
4. Ghosh, S. In *CRC Hand Book of Organic Photochemistry and Photobiology*; Horspool, W. M., Lenci, F., Eds.; CRC Press: Boca Raton, Florida, 2004; pp 1–24. Chapter 18.
5. For Cu(I)-catalyzed [2+2] photocycloaddition reactions see: (a) Salomon, R. G.; Ghosh, S.; Zagorski, M. G.; Reitz, M. *J. Org. Chem.* **1982**, *47*, 829; (b) Salomon, R. G.; Coughlin, D. J.; Ghosh, S.; Zagorski, M. G. *J. Am. Chem. Soc.* **1982**, *104*, 998; (c) Raychowdhuri, S. R.; Ghosh, S.; Salomon, R. G. *J. Am. Chem. Soc.* **1982**, *104*, 8641; (d) Avasthi, K.; Raychaudhuri, S. R.; Salomon, R. G. *J. Org. Chem.* **1984**, *49*, 4322; (e) Salomon, R. G.; Ghosh, S.; Raychowdhuri, S. R.; Miranti, T. S. *Tetrahedron Lett.* **1984**, *25*, 3167; (f) Salomon, R. G.; Ghosh, S. *Synthesis* **1984**, *62*, 125; (g) Ghosh, S.; Raychowdhuri, S. R.; Salomon, R. G. *J. Org. Chem.* **1987**, *52*, 83; (h) Salomon, R. G.; Sachinvala, N. D.; Roy, S.; Basu, B.; Raychaudhuri, S. R.; Miller, D. B.; Sharma, R. B. *J. Am. Chem. Soc.* **1991**, *113*, 3085; (i) Salomon, R. G.; Basu, B.; Roy, S.; Sachinvala, N. D. *J. Am. Chem. Soc.* **1991**, *113*, 3096; (j) Langer, K.; Mattay, J. *J. Org. Chem.* **1995**, *60*, 7256; (k) Holt, D. J.; Barker, W. D.; Jenkins, P. R.; Ghosh, S.; Russel, D. r.; Fawcell, J. *Synlett* **1999**, 1003; (l) Galoppini, E.; Chebolu, R.; Gilardi, R.; Zhang, W. *J. Org. Chem.* **2001**, *66*, 162; (m) Bach, T.; Spiegel, A. *Eur. J. Org. Chem.* **2002**, *4*, 645; (n) Bach, T.; Spiegel, A. *Synlett* **2002**, 1305; (o) Braun, I.; Rudroff, F.; Mihovilovic, M. D.; Bach, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 5541.
6. (a) Ghosh, S.; Patra, D.; Saha, G. *J. Chem. Soc., Chem. Commun.* **1993**, 783; (b) Ghosh, S.; Patra, D. *Tetrahedron Lett.* **1993**, *34*, 4565; (c) Patra, D.; Ghosh, S. *J. Org. Chem.* **1995**, *60*, 2562; (d) Patra, D.; Ghosh, S. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2635; (e) Ghosh, S.; Patra, D.; Samajdar, S. *Tetrahedron Lett.* **1996**, *37*, 2073; (f) Haque, A.; Ghatak, A.; Ghosh, S.; Ghoshal, N. *J. Org. Chem.* **1997**, *62*, 5211; (g) Samajdar, S.; Patra, D.; Ghosh, S. *Tetrahedron* **1998**, *54*, 1789; (h) Panda, J.; Ghosh, S. *Tetrahedron Lett.* **1999**, *40*, 6693; (i) Samajdar, S.; Ghatak, A.; Ghosh, S. *Tetrahedron Lett.* **1999**, *40*, 4401; (j) Ghosh, S.; Banerjee, S. P.; Chowdhury, K.; Mukherjee, M.; Howard, J. A. K. *Tetrahedron Lett.* **2001**, *42*, 5997; (k) Bannerjee, S.; Ghosh, S. *J. Org. Chem.* **2003**, *68*, 3981; (l) Sarkar, N.; Nayek, A.; Ghosh, S. *Org. Lett.* **2004**, *6*, 1903; (m) Malik, C. K.; Vaultier, M.; Ghosh, S. *Synthesis* **2007**, 1247.
7. *General experimental procedure for photochemical reaction*:
General procedure is illustrated by the synthesis of the acetal **2**: (1*S*,3a'*R*,5*S*,5'*S*,6*R*,6a'*R*)-2',2'-dimethyl-5'-(2-methyl-1,3-dioxolan-4-yl)dihydro-3a'*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-*d*][1,3]dioxole] (**2**). A solution of the diol **1** (500 mg, 1.74 mmol) in dry diethyl ether (dried by distillation over Na-benzophenone under Ar atmosphere) (120 mL) was poured into a pyrex cell. The ethereal solution was then degassed by bubbling Ar gas through it for 30 min. Freshly prepared $(CuOTf)_2{\cdot}C_6H_6$ (76 mg, 0.26 mmol) was added to the reaction mixture. The reaction mixture was then irradiated internally under a positive pressure of Ar with a Hanovia 450 W medium pressure mercury vapor lamp through a water-cooled quartz immersion well for about 4 h. After completion (TLC), the reaction mixture was poured into ice cold ammonia solution (10 mL, 35%) in a separatory funnel. After thoroughly shaking, the blue colored aqueous layer was separated. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and finally evaporation of the solvent in vacuo afforded an oil. The crude mass was then purified through column chromatography over silica-gel using petroleum ether–diethyl ether (9:1) as the eluent to provide the acetal **2** (mixture of two diastereoisomers, ca. 2:1) (354 mg, 65%) as light yellow oil. $[\alpha]_D^{26}$ 89.8 (*c* 1.77, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) (mixture of two diastereoismers, ca. 2:1) δ 5.55 (1H, d, J = 3.9 Hz), 5.53 (1H, d, J = 3.3 Hz), 5.17 (1H, q, J = 4.8 Hz), 5.05 (1H, q, J = 4.8 Hz), 4.55 (2H, t, J = 3.2 Hz), 4.45 (2H, d, J = 9.9 Hz), 4.30–4.13 (2H, m), 4.08–3.94 (4H, m), 3.91–3.77 (5H, m), 3.48–3.38 (5H, m), 3.02–2.90 (4H, m), 2.29–2.19 (2H, m), 1.48 (6H, s), 1.41 (3H, d, J = 4.8 Hz), 1.38 (3H, d, J = 4.8 Hz), 1.29 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of two diastereomers) δ 112.4, 112.3, 103.8, 103.6, 102.4, 102.1, 86.2, 85.9, 82.6, 81.0, 74.8, 73.8, 73.7, 73.6, 70.8, 70.7, 70.2, 69.6, 48.6, 48.5, 41.6, 41.3, 35.1 (2CH), 28.1, 28.0, 27.1, 27.0, 26.6, 26.5, 20.2, 20.1; HRMS (ESI) calcd for $C_{16}H_{24}O_6Na$ $(M+Na)^+$, 335.1471; found, 335.1472.
8. All new compounds were characterized through ^1H, ^{13}C NMR, and HRMS spectroscopy.
9. Fischer, J.-C.; Horton, D. *Carbohydr. Res.* **1977**, *59*, 477.
10. Wuts, P. G. M.; Greene, T. W. *Protective Groups in Organic Synthesis*, 4th ed.; Wiley Interscience, 2007. pp 16–366, Chapter 2.
11. (a) Stevens, I. D. R.; Watts, C. T. *J. Chem. Soc., Chem. Commun.* **1965**, 259; (b) Kulevsky, N.; Wang, C. T.; Stenberg, V. I. *J. Org. Chem.* **1969**, *34*, 8647; (c) Shah, A.; George, M. V. *Tetrahedron* **1971**, *27*, 1291.
12. cf. Woodhouse, M. E.; Lewis, F. D.; Marks, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 996.
13. Baciocchi, E.; Bietti, M.; Lanzalunga, O. *J. Phys. Org. Chem.* **2006**, *19*, 467.
14. (a) Lin, W.; Lawrence, D. S. *J. Org. Chem.* **2002**, *67*, 2723; (b) Balnc, A.; Bochet, C. G. *J. Org. Chem.* **2003**, *68*, 1138; (c) Kostikov, A. P. *Org. Lett.* **2008**, *10*, 5277. and references cited therein; (d) Šebej, P.; Šolomek, T.; Hroudná, L.; Brancová, P.; Klán, P. *J. Org. Chem.* **2009**, *74*, 8647. and references cited therein.