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SYNTHESIS OF MULTICYCLIC PYRROLIDINES VIA COPPER(I) CATALYZED PHOTOBICYCLIZATION OF ETHYL N,N-DIALLYL CARBAMATES[1]

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Abstract. Ultraviolet irradiation of ethyl N,N-diallylcarbamates in the presence of copper(I) trifluoromethanesulfonate (CuOTf) catalyst results in photobicyclization to give bi or tricyclic pyrrolidines incorporating the N-carboethoxy-3-azabicyclo[3.2.0]heptane moiety.

In principle the utility of olefin photoreactions[2] for synthesis of complex organic molecules can be limited by the ultraviolet absorptions of functional substituents. We have discovered a remarkable dichotomy in the behavior of N,N-diallyl amides and carbamates which may be a consequence of the different ultraviolet absorptions of these functional groups. Thus, N,N-diallylacetamide (1a) or N,N-diallylformamide (1b) remained virtually unchanged[3] upon ultraviolet irradiation of an 0.1 M solution in diethyl ether containing 5 mole% CuOTf.[4] In dramatic contrast, similar treatment of ethyl N,N-diallylcarbamate (1c) resulted in complete consumption of the latter and production of N-carboethoxy-3-azabicyclo[3.2.0]heptane (2c) which was isolated in 74% yield (see Table I).

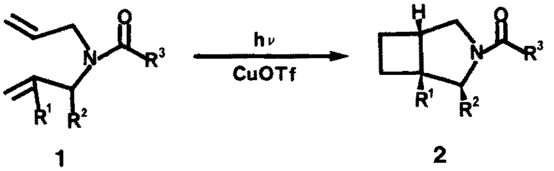
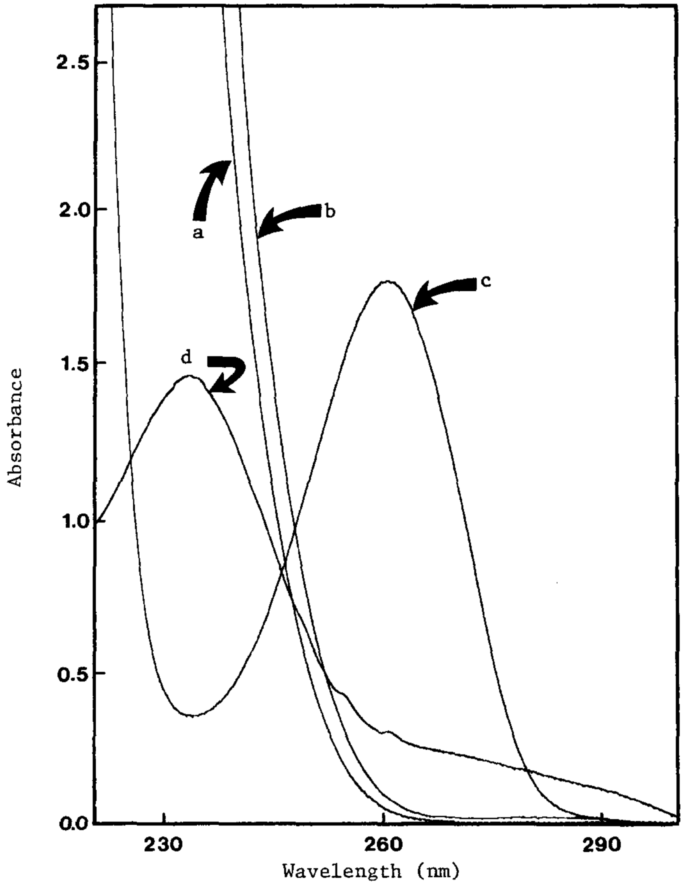


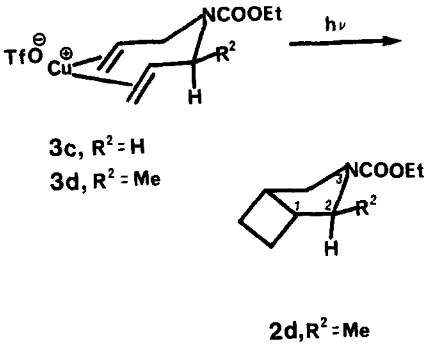
Table I. Copper Catalyzed Photobicyclization of N,N-Diallylamides and N,N-Diallylcarbamates (1)[a]

1	R^1	R^2	R^3	Reaction Time (h)	2 (Yield %)	ε[b]
a[c]	H	H	Me	24	0[h]	192
b[d]	H	H	H	24	0[h]	231
c[e]	H	H	OEt	24	74	15
d[f]	H	Me	OEt	48	60	-
e[g]	Me	H	OEt	22	76	-

(a) 0.04 to 1.0M solutions in diethyl ether with 5 to 10 mole% CuOTf as catalyst. (b) Molar extinction at 233.4 nm. (c) Prepared by acetylation of diallylamine with acetyl chloride. (d) Prepared by formylation of diallylamine with ethyl formate. (e) Prepared by carboethoxylation of diallylamine with ethyl chloroformate. (f) Prepared by β-methallylation of ethyl N-allylcarbamate with β-methallyl bromide. (g) Prepared by α-methallylation of ethyl N-allylcarbamate with 3-chlorobut-1-ene. (h) Nearly quantitative recovery of starting N,N-diallylamide.

Figure 1 shows the ultraviolet spectra of 1a-1c as well as that of a 1:1 mixture of 1c with CuOTf. Typically CuOTf-alkene complexes containing one, two, three, or even four coordinated C=C bonds exhibit ultraviolet absorption at 235 ± 5 nm (ε_{max} 2,950 ± 450).[2] The 1:1 complex of 1c with CuOTf, which probably has a chelate structure 3c, is no exception, exhibiting λ_{max} = 233.4 nm (ε_{max} = 2,676). While the amides 1a and 1b show substantial end absorptions with $\varepsilon \approx 200$ at this wavelength, the ultraviolet spectrum of 1c has a trough at precisely this wavelength (ε_{min} 15). Thus it is tempting to speculate that the acetamide and formamide functional groups competitively inhibit photocycloaddition by consuming photons in the 233 nm region which are essential for photoactivation of the copper(I)-bisalkene complex. Further study is required to firmly establish the validity of this hypothesis.





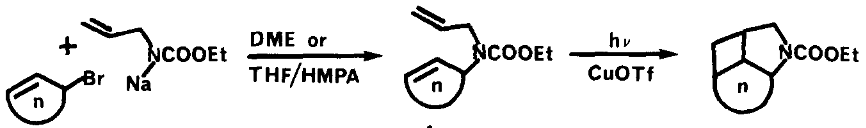
3c, R^2=H
3d, R^2=Me

2d, R^2=Me

Figure 1. Ultraviolet absorption spectra of solutions in diethyl ether: (a) 2.1×10^{-2}M N,N-diallylacetamide (1a), (b) 2.1×10^{-2}M N,N-diallylformamide (1b), (c) 2.1×10^{-2}M ethyl N,N-diallylcarbamate (1c), (d) 5.3×10^{-4}M ethyl N,N-diallylcarbamate·CuOTf (3c).

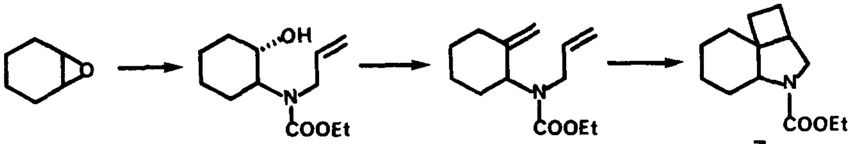
At present, however, it is already apparent that copper(I) catalyzed photobicyclization of N,N-diallylcarbamates is widely applicable for a novel C-C connective synthesis of bi and tricyclic pyrrolidines incorporating the 3-azabicyclo[3.2.0]heptane ring system. The product 2d is especially interesting (see Table I). Both ^{1}H and ^{13}C NMR spectra[5] show that 2d is a single isomer presumably with the C-2 methyl substituent in the exo configuration. The stereoselectivity of the 1d → 2d conversion[6], which should be valuable for applications of such photobicyclizations in organic synthesis, is probably the result of a preference for an intermediate copper(I) complex 3d with an equatorial methyl substituent. An axial methyl substituent would experience severe crowding of the cis-terminal vinyl hydrogen.

The unsymmetrical N,N-diallyl carbamates 1d and 1e were prepared by allylation of ethyl N-allylcarbamate. Monocyclic unsymmetrical N,N-diallylcarbamates 4a and 4b, prepared similarly, afford tricyclic photobicyclization products 5a and 5b respectively. The N,N-diallylcarbamate 6, prepared from cyclohexene oxide,[7] did not give the tricyclic carbamate 7 upon ultraviolet irradiation in the presence of a catalytic amount of CuOTf in ether solution. Prolonged irradiation of the ether solution afforded nonvolatile presumably polymeric products. Fortunately, ultraviolet irradiation of 6 with a catalytic amount of CuOTf in benzene solution afforded 7 in 47% yield.[8]



4a, n = 6
4b, n = 7

5a, n = 6 (53%)
5b, n = 7 (50%)



6

7

Functional substituents enhance the potential utility of olefin photoreactions in organic synthesis. Previous studies showed that copper(I) catalyzed photobicyclization is feasible for substrates incorporating homoallyl,[1] allyl,[1,9] and vinyl[1] ether, as well as homoallyl,[9] and allyl[10] alcohol, and aryl[8] groups. The present study extends this list to include allylic carbamates. In contrast, the acetamide and formamide functional groups apparently inhibit copper(I) catalyzed photobicyclization.

Typical Procedures

Allylation of Ethyl N-Allylcarbamate:

Sodium hydride (20 mmole), obtained by washing a 57% suspension in mineral oil (0.85 g) with dry pentane (2 x 5 mL), was suspended in dry 1,2-dimethoxyethane (20 mL) under dry nitrogen. Ethyl N-allylcarbamate[11] (2.6 g, 20 mmole) was added dropwise with magnetic stirring at room temperature. Stirring was continued for an additional 3 h. Then 3-bromo-2-methylbut-1-ene (3.24 g, 24 mmoles) was added and the resulting mixture stirred 20 h at room temperature and then boiled 2 h under reflux. After cooling, water (40 mL) and 10% HCl (20 mL) were added and the mixture extracted with ether (4 x 10 mL). The extract was washed with water (10 mL), dried ($MgSO_4$), and solvent was removed by rotary evaporation. Distillation of the residual oil afforded ethyl N-allyl-N-methallylcarbamate (1d) (3.0 g, 83%) as a colorless oil, b.p. 108-110°C/20 mm.

Photobicyclization of an N,N-Diallylcarbamate:

A solution of 1d (2.9 g, 16 mmoles) and $(CuOTf)_2C_6H_6$[4] in ether (400 mL, freshly distilled from NaH) was stirred magnetically and irradiated 22 h with a 450 watt Hanovia medium pressure mercury arc through a water cooled internal quartz immersion well in a cylindrical pyrex vessel. The resulting solution was washed with a mixture of ice (100 g) and concentrated aqueous NH_4OH (100 mL), then saturated aqueous NaCl (100 mL), dried ($MgSO_4$), and solvent was removed by rotary evaporation. Distillation of the residual oil afforded N-carboethoxy-1-methyl-3-azabicyclo-[3.2.0]heptane (2d) (2.2 g, 74%) as a colorless oil, b.p. 115-122°C/12 mm.

Acknowledgement: We thank the National Science Foundation for generous support of our research.

References and Notes

1. Copper(I) Catalysis of Olefin Photoreactions. 12. For paper 11 in this series see: Raychaudhuri, S.R.; Ghosh, S.; Salomon, R.G. J. Am. Chem. Soc. 1982, 104, 6851.
2. For a recent review see: Salomon, R.G. Tetrahedron 1983, 39, 485.

3. Prolonged irradiation (1 to 2 weeks) eventually results in complete consumption of the N,N-diallylamides. However, rather than the desired bicyclic products, nonvolatile, presumably polymeric products are formed.
4. Salomon, R.G.; Kochi, J.K. J. Am. Chem. Soc. 1973, 95, 1889.
5. ^1H NMR (200 MHz, $CDCl_3$) δ 1.15(3H,t,J=6.9Hz), 1.17(3H,D,J=6.4Hz), 1.42-1.60(H), 1.72-2.19 (3H), 2.60-2.78(H,C_1-H), 2.86(H,m,C_5-H), 3.31(H,dd,J=11.5,4.3Hz,C_4-H_{endo}), 3.61(H,dd,J=11.5, 8.1Hz,C_4-H_{exo}), 3.72(H,apparent quintet,J=6.4Hz,C_2-H), 4.03(H,q,J=6.9Hz,$OC\underline{H}_2CH_3$), 4.05(H, q,J=6.9Hz,$OC\underline{H}_2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.8, 16.0, 19.3, 24.3, 36.6, 43.7, 53.7, 56.2, 60.7, 155.9.
6. We recently discovered similar stereoselectivity in copper(I) catalyzed photobicyclizations of α-substituted diallyl ethers.[1]
7. Details of this synthesis will be presented in a subsequent full paper.
8. The use of this solvent for copper(I) catalyzed photobicyclization was first reported by Wilcox, R.D.; Pagni, B.M.; Hassaneen, H.M.; Kabalka, G.W. J. Org. Chem. 1981, 46, 1931.
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