pounds I and II are (to our knowledge) novel since they contain carbon-to-carbon bonds that cleave by merely dissolving them in solution.

The thermodynamics of carbon–carbon bond formation is related closely to the $pK_{HA}$ and $pK_{R^+}$ of the carbanion and carbocation. For para-substituted arylmalononitrile carbanions reacting with substituted cyclopropenium ions the Brønsted basicity of the carbanions was related linearly to their basicities toward the carbocations (e.g., Lewis basicities). The apparent (irreversible) oxidation potentials were also proportional to the Lewis basicities of the anions toward the triphenylcyclopropenium ion.

Preliminary kinetic studies[8] indicate that carbanion–carbocation reactions are affected by the stabilities and ion pairing of the carbanions and carbocations. The relation between kinetics and thermodynamics will be a primary area for our future research.

The effect of solvent on the heterolytic equilibria of compounds I and II follows the Born equation and the Debye–Hückel limiting law and provides a starting point for a more extensive investigation of the solvation of less stable carbocations and carbanions.

Some carbanions and carbocations reacted by electron transfer in a pattern related to their redox potentials. Electron transfer appeared to be more sensitive to substituent variation than was coordination. Thus, the likelihood of electron transfer instead of simple coordination increases as the stability of the carbocation and carbanion decreases. Since both reactions are highly sensitive to solvent polarity, it may be possible to control the competition between bond formation by coordination vs. electron transfer through suitable choice of medium.

**Acknowledgment.** We are pleased to acknowledge support for this work from NSF Grant CHE-8006202 the assistance of Professors C. W. Anderson and A. T. McPhail and helpful suggestions by Professor C. D. Ritchie.

**Registry No.** $CH_3CH_2CH(C(O)OMe)_2$, 26717-67-9; $CH_3CH_2CH(CO_2H)_2$, 601-75-2; $CH_3CH(C(O)OMe)_2$, 609-02-9; $CH_3CH(CO_2H)_2$, 516-05-2; $CH_3C(O)CH_3$, 67-64-1; $CH_3C(O)(CH_3)HC(O)CH_3$, 815-57-6; $CH_3C(O)CH_2C(O)CH_3$, 123-54-6; $CH_3C(O)C(Et)HC(O)CH_3$, 1540-34-7; $HO_2CCH_2C(CH_3)_2CH_2CO_2H$, 4839-46-7; $CH_3(CH_2)_2C(O)CH_2C(CH_3)_2CH_2C(O)OEt$, 91879-91-3; $p$-$NO_2C_6H_4CH(CN)_2$, 7077-65-8; $p$-$NO_2C_6H_4CH_2CN$, 555-21-5; $p$-$ClC_6H_4CH(CN)_2$, 32122-64-8; $p$-$ClC_6H_4CH_2CN$, 140-53-4; $p$-$ClC_6H_4CHCN^-Na^+$, 60389-37-9; PhOCN, 1122-85-6; $p$-$CNC_6H_4CH(CN)_2$, 91879-92-4; $p$-$MeC_6H_4CH(CN)_2$, 33534-88-2; $p$-$MeOC_6H_4CH(CN)_2$, 33534-87-1; $PhCH(CN)_2$, 3041-40-5; PhOH, 108-95-2; $p$-$CNC_6H_4C(CN)_2^-$, 91880-06-7; $p$-$CNC_6H_4C(CN)_2^-K^+$, 91879-93-5; $p$-$ClC_6H_4C(CN)_2^-$, 91880-07-8; $p$-$ClC_6H_4C(CN)_2^-K^+$, 87658-34-2; $p$-$MeC_6H_4C(CN)_2^-$, 91880-08-9; $p$-$MeC_6H_4C(CN)_2^-K^+$, 87658-35-3; $p$-$MeC_6H_4C(CN)_2CH_3$, 91879-94-6; $p$-$MeOC_6H_4C(CN)_2^-$, 85535-17-7; $p$-$MeOC_6H_4C(CN)_2^-K^+$, 91879-95-7; $PhC(CN)_2^-$, 45884-26-2; $PhC(CN)_2^-K^+$, 91879-96-8; $p$-$NO_2C_6H_4C(CN)_2^-$, 56577-73-2; $p$-$NO_2C_6H_4C(CN)_2^-K^+$, 20394-72-3; $p$-$NO_2C_6H_4C(CN)_2^-Bu_4N^+$, 91879-97-9; $Bu_4NOH$, 2052-49-5; $(p$-$MeC_6H_4)_3COH$, 3247-00-5; $p$-$MeC_6H_4MgBr$, 4294-57-9; $p$-$MeC_6H_4C(O)OMe$, 99-75-2; $(p$-$MeC_6H_4)_3C^+BF_4^-$, 1650-48-2; $(p$-$MeOC_6H_4)_3COH$, 3010-81-9; $p$-$MeOC_6H_4MgBr$, 13139-86-1; $p$-$MeOC_6H_4C(O)OMe$, 121-98-2; $(p$-$MeOC_6H_4)C^+BF_4^-$, 437-30-9; $(CH_3)_3CC(O)C[(p$-$MeC_6H_4)_3C]HC(O)C(CH_3)_3$, 19672-57-2; dimedone, 126-81-8; 2-methyldimedone, 1125-11-7; 2-ethyldimedone, 2406-29-3; methyl Meldrum's acid, 3709-18-0; ethyl Meldrum's acid, 17216-65-8; $p$-$NO_2C_6H_4C(CN)_2C(CN)_2C_6H_4$-$p$-$NO_2$, 7061-41-8; triphenylcyclopropene, 16510-49-9; triphenylcyclopropenylium, 12190-17-9; triphenylcyclopropenylium tetrafluoroborate, 741-16-2; trimethylcyclopropenylium, 26827-04-3; trimethylcyclopropenylium tetrafluoroborate, 30109-53-6; tropylium tetrafluoroborate, 27081-10-3; (1,2,3-triphenylcyclopropenyl)($p$-nitrophenyl)malononitrile, 86943-83-1; (1,2,3-triphenylcyclopropenyl)($p$-cyanophenyl)malononitrile, 91879-98-0; (1,2,3-triphenylcyclopropenyl)($p$-methylphenyl)malononitrile, 91879-99-1; (1,2,3-trimethylcyclopropenyl)($p$-nitrophenyl)malononitrile, 86943-82-0; (1,2,3-trimethylcyclopropenyl)($p$-chlorophenyl)malononitrile, 91880-00-1; (1,2,3-trimethylcyclopropenyl)($p$-cyanophenyl)malonitrile, 91880-01-2; (1,2,3-trimethylcyclopropenyl)($p$-methylphenyl)malononitrile, 91880-02-3; (1,2,3-trimethylcyclopropenyl)($p$-methoxyphenyl)malononitrile, 91880-03-4; (1,2,3-trimethylcyclopropenyl)phenylmalononitrile, 91880-04-5; 4-tropyl-2,2,6,6-tetramethyl-3,5-heptanedione, 91880-05-6; cyanogen chloride, 506-77-4.

# Novel Bicycloannulation via Tandem Vinylation and Intramolecular Diels–Alder Reaction of Five-Membered Heterocycles: A New Approach to Construction of Psoralen and Azapsoralen

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*Received March 19, 1984*

**Abstract:** *trans*-4-(Phenylsulfinyl)-3-buten-2-one (**1**) was found to undergo a new versatile addition–elimination reaction with five-membered compounds such as furans, pyrroles, imidazole, pyrazole, and 6-(dimethylamino)fulvene to give an excellent yield of the corresponding *trans*-4-aryl-3-buten-2-ones (**3**). The thermal reaction of the propargyl ethers **7a,b** prepared from **3a,b** gave a single intramolecular Diels–Alder adduct, **8a,b**, in 59% and 38% yields, respectively. Treatment of **7a,b** with *t*-BuOK in refluxing *tert*-butyl alcohol afforded another type of Diels–Alder adduct, **10a,b**, in almost quantitative yields. This bicycloannulation strategy was applied to a new synthesis of psoralen which is of current interest due to its unique photoreactivity with DNA. The acid-catalyzed reaction of sulfoxide **12**, prepared from ethyl acetoacetate in high yield, with furan gave **13** in 78% yield. The intramolecular Diels–Alder reaction of the neopentyl acetal of **13** in the presence of Pd/C followed by acid hydrolysis afforded the tricyclic ketone **18** in 38% yield. Baeyer–Villiger oxidation and dehydrogenation of **18** completed the synthesis of psoralen (**11**). Futhermore, hitherto unknown azapsoralen **20** was also synthesized by this method.

The widespread occurrence of linearly fused heterocyclic [5.6.*n*] ring systems in natural products stimulates the development of new strategies.[1] A potentially very versatile approach envisions an intramolecular Diels–Alder reaction[2] of heterocyclic aromatic compounds possessing a 2-vinyl substituent (i.e., A) and a subsequent aromatization to give B as outlined in eq 1. The key to

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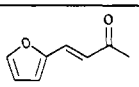
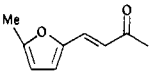
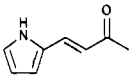
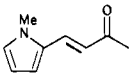
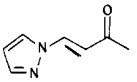
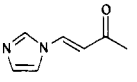
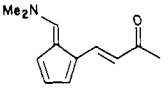
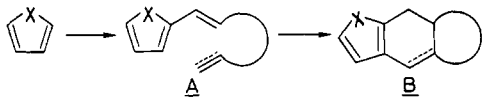
**Table I.** Addition–Elimination Reactions of *t*-SBO (**1**) with Five-Membered Aromatic Compounds

| entry | substrate | condition[a] | product[b] | % yield |
|---|---|---|---|---|
| 1 |  | A, 6 days |  **3a** | 65 |
| 2 | | B, 1 day | | 82 |
| 3 |  | A, 6 days |  **3c** | 91 |
| 4 | | B, 1 h | | 86 |
| 5 |  | A, 14 h |  **3d** | 98 |
| 6 |  | A, 2 weeks |  | 18 |
| 7 | | B, 30 min | **3b** | 65 |
| 8 |  | C, 8 days |  **3e** | 92 |
| 9 |  | D, 17 h |  **3f** | 94 |
| 10 |  | D, 6 h |  **3g** | 57 |

[a] All reactions were carried out at 25 °C under the following conditions (for 1 equiv of **1**): (A) excess of substrate (~10 equiv), neat; (B) excess of substrate (~10 equiv), *p*-TsOH (catalyst), neat; (C) 1.2 equiv of substrate, $CH_3CN$; (D) 1.2 equiv of substrate, *p*-TsOH (catalyst), $CH_3CN$. [b] See ref 4.

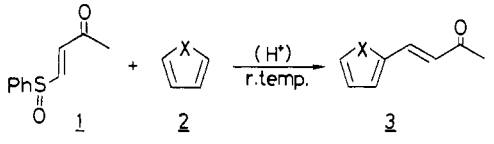


(1)

this sequence was to device a general method of synthesis of compounds A. We wish to report a new versatile way of introducing an enone moiety to heterocyclic aromatic rings and its utility in forming heterocyclic [5.6.*n*] ring systems especially with respect to the intramolecular Diels–Alder reaction. Furthermore, this methodology has been successfully applied to the synthesis of a naturally occurring furocoumarin, psoralen (**11**),[3] and its hitherto unknown aza analogue **20**.

## Results and Discussion

**Addition–Elimination Reaction.** In the course of our studies of pericyclic reactions of sulfur-activated olefins, we have found a novel and very facile addition–elimination reaction of *trans*-4-(phenylsulfinyl)-3-buten-2-one (**1**) with five-membered heterocycles **2**, giving a high yield of *trans*-4-(2-aryl)-3-buten-2-one (**3**) (eq 2). Compound **1**, mp 71–72.5 °C, was prepared from



(2)

an *E*/*Z* mixture of 4-(phenylthio)-3-buten-2-one[4] by treatment with *m*-CPBA (1 equiv) in $CH_2Cl_2$ followed by column chromatography on silica gel which caused a complete isomerization to the *E*-isomer. When a mixture of 1 equiv of **1** and an excess (~10 equiv) of furan were stirred in the presence of a catalytic amount of *p*-toluenesulfonic acid at room temperature (1 day), compound **3a** (X = O)[5] was obtained in 82% yield as a sole product. This reaction also took place without any acid catalyst but much slowly and needed a longer reaction time. Table I summarizes the results with other heterocyclic compounds. The reaction proceeded with extraordinary ease, and some of these products are otherwise difficult to obtain. The site selectivities and stereoselectivities of these reactions are also noteworthy. The trans stereochemistry of these products was clearly indicated by the large coupling constant (14–16 Hz) between two olefinic protons in the $^1H$ NMR spectra (Table II). The formation of **3** can be reasonably explained by the initial Michael-type addition[6] of **2** at its most nucleophilic position (having the largest HOMO coefficient)[7] to **1** followed by the elimination of sulfenic acid. In accord with this, the similar reaction of *trans*-4-(phenylsulfonyl)-3-buten-2-one (**4**) with *N*-methylpyrrole afforded 4-(*N*-methyl-2-pyrrolyl)-4-(phenylsulfonyl)-2-butanone (**5**), the Michael-type adduct, in 74% yield together with an 1:2 adduct

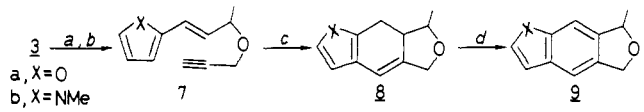
**Table II.** Physical Properties and Spectral Data for **3**, **5**, and **6**

| compd | mp, °C | IR,[a] $cm^{-1}$ | $^1H$ NMR,[b] $\delta(CDCl_3)$ |
|---|---|---|---|
| **3a** | | 1695, 1670 | 7.48 (1 H, dm, *J* = 1.8), 7.26 (1 H, d, *J* = 16.0), |
| | | 1620, 1560 | 6.66 (1 H, d, *J* = 3.6), 6.60 (1 H, d, *J* = 16.0), |
| | | 1480 | 6.47 (1 H, dd, *J* = 3.6, 1.8), 2.33 (3 H, s) |
| **3c** | | 1690, 1665 | 7.19 (1 H, d, *J* = 15.8), 6.57 (1 H, d, *J* = 3.2), |
| | | 1620, 1580 | 6.53 (1 H, d, *J* = 15.8), 6.11 (1 H, dm, *J* = 3.2), |
| | | 1530 | 2.36 (3 H, s), 2.31 (3 H, s) |
| **3d** | 113–115 | 3480, 3400–3200, 1670 | 10.4–9.00 (1 H, br, s), 7.45 (1 H, d, *J* = 16.2), 7.00 (1 H, m), 6.61 (1 H, m), 6.43 (1 H, d, *J* = 16.2), |
| | | 1620, 1600 | 6.29 (1 H, m), 2.33 (3 H, s) |
| **3b** | | 1670, 1620 | 7.49 (1 H, d, *J* = 16.0), 6.9–6.6 (2 H, m), |
| | | 1600 | 6.49 (1 H, d, *J* = 16.0), 6.20 (1 H, dd, *J* = 3.6, 2.4), 3.73 (3 H, s), 2.31 (3 H, s) |
| **3e** | | 1700, 1680 | 7.92 (1 H, d, *J* = 14.0), 7.74 (1 H, s), 7.72 (1 H, d, *J* = 2.6) 6.69 (1 H, d, *J* = 14.0), 6.47 (1 H, dd, *J* = 2.6, 1.6), 2.34 (3 H, s) |
| **3f** | 111.5–114.5 | 1710, 1680 | 7.82 (1 H, d, *J* = 14.0), 7.81 (1 H, s), 7.24 (2 H, m), |
| | | 1645, 1625 | 6.40 (1 H, d, *J* = 14.0), 2.36 (3 H, s) |
| **3g** | 130–130.5 | 1620, 1600 | 7.68 (1 H, d, *J* = 15.6), 7.57 (1 H, s), |
| | | 1570 | 6.93 (1 H, dd, *J* = 3.0, 2.0), 6.82 (1 H, dd, *J* = 4.08 2.0), 6.58 (1 H, dd, *J* = 4.0, 3.0), 6.52 (1 H, d, *J* = 15.6), 3.36 (6 H, s), 2.30 (3 H, s) |
| **5** | | 1740, 1320 | 7.51 (5 H, m), 6.45 (1 H, 7), 6.06 (2 H, m), |
| | | 1165 | 4.80 (1 H, dd, *J* = 9.0, 4.1), 3.23 (3 H, s), 3.36 (2 H, m), 2.16 (3 H, s) |
| **6** | | 1720 | 6.49 (2 H, dd, *J* = 2.4, 1.9)8 6.01 (2 H, dd, *J* = 3.5, 2,8), 5.85 (2 H, m), 4.59 (1 H, t, *J* = 7.0), 3.45 (6 H, s), 3.06 (2 H, d, *J* = 7.0), 2.10 (3 H, s) |

[a] $CHCl_3$ for **3b**, **3c**, **3d**, **3e**, **3f**, **3g**, and **5**. Neat for **3a** and **6**. [b] *J* values in hertz.

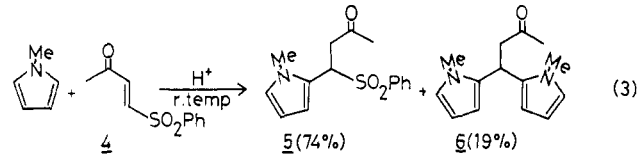
(1) Glasby, J. S. "Encyclopedia of the Terpenoids"; Wiley: New York, 1982.
(2) For a review, see: Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63.
(3) Jois, H. S.; Manjunath, B. L.; Rao, S. V. *J. Indian Chem. Soc.* **1933**, *10*, 41. For examples of previous synthesis, see: (a) Esse, R. C.; Christensen, B. E. *J. Org. Chem.* **1960**, *25*, 1565. (b) Dann, O.; Volz, D. *Arch. Pharm.* **1975**, 121 and references cited therein.
(4) Bakuzis, P.; Bakuzis, M. L. F. *J. Org. Chem.* **1981**, *46*, 235.
(5) Claisen, L. *Ber.* **1881**, *14*, 2469.
(6) Diels, O.; Alder, K. *Liebigs Ann. Chem.* **1931**, *490*, 267.
(7) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976.

Scheme I[a]

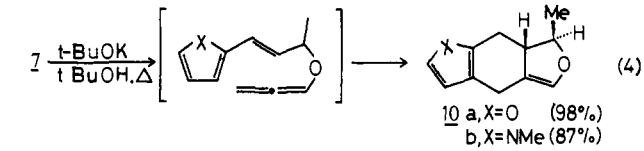



[a] (a) $NaBH_4$, MeOH, 0 °C. (b) *n*-BuLi, $Me_2SO$, $C_6H_6$, then $CH{\equiv}CCH_2Br$, 0 °C. (c) Toluene, sealed tube, 150 °C. (d) DDQ, $C_6H_6$, 25 °C (or Pd/C, AcOEt, ⇌).

**6** (19%) (eq 3). These results indicate that the phenylsulfinyl group in **1** is important for the facile formation of **3** under the mild reaction conditions.




**Intramolecular Diels–Alder Reactions.** With thus easily available **3**, the validity of the strategy shown in eq 1 was investigated. Compounds **3a** (X = O) and **3b** (X = NMe) were first converted to the propargyl ethers **7a,b** in 70–80% yields and then subjected to the thermal reaction at 150 °C (toluene, sealed tube) to give the Diels–Alder adducts **8a,b** in 59% and 38% yields, respectively, as a single product (Scheme I). These adducts could be easily converted to the corresponding aromatic compounds **9** by treating with DDQ in benzene or refluxing with Pd/C in ethyl acetate. In contrast, treatment of **7a,b** with *t*-BuOK in refluxing *t*-BuOH (83 °C) resulted in the smooth formation of another type of Diels–Alder adducts, **10a,b** in almost quantitative yields, probably via allenyl ether intermediates[8] (eq 4). The facility of




these reactions can therefore be attributed to the favorable geometry of the allenyl ether for the intramolecular Diels–Alder reactions compared with that of the propargyl ether as shown in Figure 1. The allenyl ether experiences no 1,3-diaxial interaction between $\alpha$- and $\alpha'$-hydrogens in these reactions due to its perpendicular structure.

The structure of all these compounds could be confirmatively determined on the basis of the spectroscopic data (see Experimental Section).

**Synthesis of Psoralen and Azapsoralen.** The integration of the above methodologies has led to a new synthesis of a naturally occurring furocoumarin, psoralen (**11**)[3] (Scheme III), which is of current interest because of its unique photoreactions with DNA[9,10] and its utility as a photochemotherapeutic agent.[11] The requisite *trans*-1-(phenylsulfinyl)-1-hepten-6-yn-3-one (**12**), mp 83–84 °C, was readily prepared from ethyl acetoacetate as shown in Scheme II. The acid-catalyzed reaction of **12** with furan proceeded smoothly at room temperature to give **13** in 78% yield (Scheme III). The trans geometry of the enone moiety was confirmed by the $^1H$ NMR spectrum ($J$ = 15.6 Hz). While all attempts for the intramolecular Diels–Alder reactions of **13** failed, its ketal derivatives underwent thermal cyclization. When the neopentyl acetal **14** prepared from **13** ($(CH_3)_2C(CH_2OH)_2$), *p*-TsOH, $C_6H_6$, reflux; 74%) was heated at 200 °C in toluene (sealed tube, 12 h), only the benzofuran derivatives **15** (57%) and **16** (3%) were formed, and none of the desired tricyclic product was obtained. However, it was found that **14**, on heating in the presence of Pd/C (200 °C, xylene, sealed tube), underwent the cycloaddition concomitant with aromatization to give **17** (Scheme III) in 38% yield together with **15** (15%) and **16** (15%).[12]

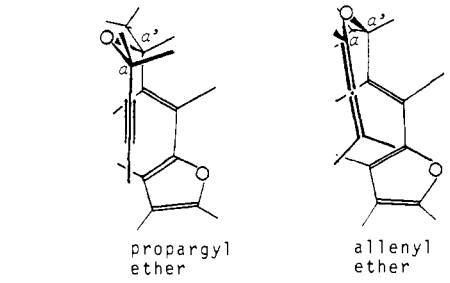
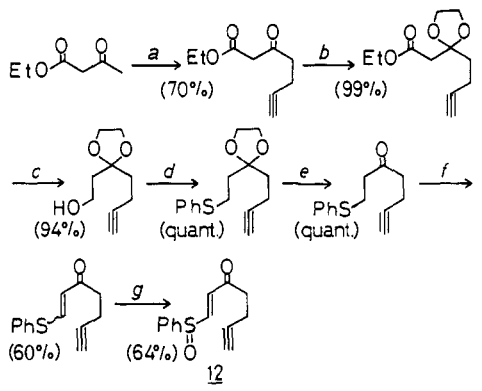


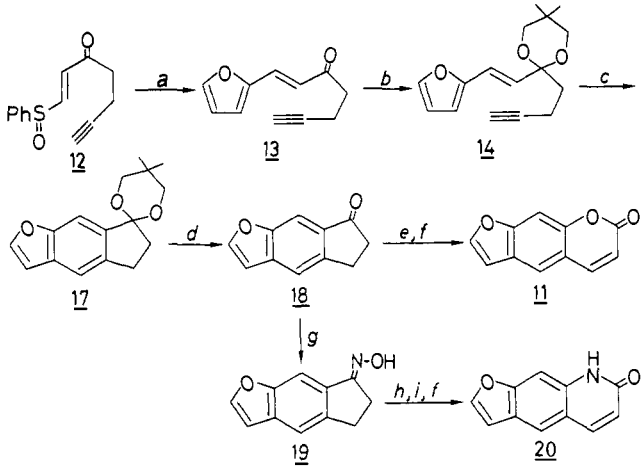

**Figure 1.**

Scheme II[a]

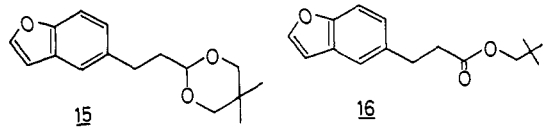



[a] (a) LDA (2 equiv), THF, then $CH{\equiv}CCH_2Br$. (b) $(CH_2OH)_2$, *p*-TsOH, $C_6H_6$, reflux. (c) LDA, ether. (d) $(PhS)_2$, *n*-$Bu_3P$, $C_6H_6$. (e) concentrated HCl, THF. (f) NCS, $C_6H_6$, then $Et_3N$. (g) *m*-CPBA, $CH_2Cl_2$, then $SiO_2$ chromatography.

Scheme III[a]




[a] (a) Excess of furan (~10 equiv), *p*-TsOH (catalyst), neat. (b) $Me_2C(CH_2OH)_2$, *p*-TsOH (catalyst), $C_6H_6$, reflux. (c) 10% Pd/C (40 w/w %), xylene, sealed tube, 200 °C. (d) *p*-TsOH (catalyst), THF, $H_2O$, room temperature. (e) 30% $H_2O_2$, excess of $Ac_2O$–concentrated $H_2SO_4$, $CH_2Cl_2$, room temperature. (f) 10% Pd/C, $Ph_2O$, reflux. (g) $H_2NOH{\cdot}HCl$, NaOAc, EtOH, reflux. (h) MsCl, $Et_3N$, $CH_2Cl_2$, 0 °C. (i) $Et_2AlCl$, $CH_2Cl_2$, −70 °C, then 5% NaOH.



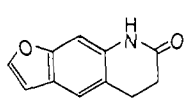

Compound **17** was quantitatively converted (*p*-TsOH, THF, $H_2O$) to the tricyclic ketone **18**, mp 146–147 °C. Baeyer–Villiger

(8) Bartlett, J.; Laird, T.; Ollis, W. D. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1315.
(9) Kanne, D.; Straub, K.; Hearst, J. E.; Rapoport, H. *J. Am. Chem. Soc.* **1982**, *104*, 6754 and references cited therein.
(10) For a review, see: Parsons, B. J. *Photochem. Photobiol.* **1980**, *32*, 813.
(11) Kornhauser, A.; Wamer, W. G.; Giles, A. L., Jr. *Science (Washington, D.C.)* **1982**, *217*, 733.

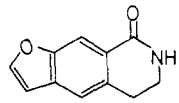
(12) The product ratio was also affected by changing the ketal moiety of **14**. The mechanistic details of these reactions will be discussed elsewhere.

oxidation of **18** (30% $H_2O$, $Ac_2O$, $H_2SO_4$, $CH_2Cl_2$)[13] followed by dehydrogenation (10% Pd/C, $Ph_2O$, reflux) completed the synthesis of psoralen (**11**) (28%, mp 160–161 °C (lit.[3] mp 161–162 °C)) identical in all respects with a sample of the natural **11** (TLC, IR, NMR, MS).[14]

All previous syntheses of psoralen started with resorcinol and its derivatives which already contain the central aromatic ring.[3] This synthesis not only provides a conceptually new route to psoralens but also possesses a wide applicability for synthesis of hetero analogues of psoralen. For example, the hitherto unknown azapsoralen **20**[15] was synthesized from the ketone **18** by a series of treatments: oximation (98%), mesylation (95), Beckmann rearrangement[16] (65%), and dehydrogenation (28%) (Scheme III). It should be noted that the Beckmann rearrangement of **19**, under the kinetic reaction conditions,[16] is essential to get the desired lactam **21** since the treatment of **19** with polyphosphoric acid at 90 °C exclusively gave the undesired isomer **22** (57%).



21



22

In conclusion, a bicycloannulation of five-membered heterocycles via a new versatile vinylation and subsequent intramolecular Diels–Alder reaction has been successfully applied to the synthesis of psoralen and azapsoralen. These results suggest the general utility of this strategy for the synthesis of the linearly fused heterocyclic [5.6.*n*] ring systems.

## Experimental Section

The melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. The UV spectra were determined with a Hitachi EPS-3T spectrophotometer. The $^1H$ NMR spectra were taken with a JEOL PS-100 spectrometer and a Hitachi R-600 spectrometer with tetramethylsilane as an internal standard, and the chemical shifts are expressed in $\delta$ values. The $^{13}C$ NMR spectra were recorded on a JEOL FX-100 with tetramethylsilane as an iternal standard. The IR spectra were taken with a JASCO IR A-1 infrared spectrometer. Mass spectra were obtained with a JEOL-O1SG double-focusing spectrometer operating at an ionization potential of 75 eV. The solid samples were ionized by electron bombardment after sublimation directly into the electron beam at 150–200 °C. Column chromatography was performed by using E. M. Merck Kieselgel 60 (70–200 mesh).

***trans*-4-(Phenylsulfinyl)-3-buten-2-one (1).** To a stirred solution of 4-(phenylthio)-3-buten-2-one (*E*/*Z* mixture)[4] (2.34 g, 13.1 mmol) in $CH_2Cl_2$ (40 mL) at 0 °C was added 80% *m*-chloroperbenzoic acid (*m*-CPBA) (2.83 g, 13.1 mmol) in portions. The resulting mixture was stirred at room temperature for 1 h and then diluted with ether, washed with aqueous $NaHCO_3$ solution, water, and brine, and dried over $Na_2SO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel with ethyl acetate/*n*-hexane (4:1) as an eluent to give **1** (2.28 g, 90%) as colorless crystals: mp 71.5–72.5 °C ($CH_2Cl_2$/*n*-hexane); IR ($CHCl_3$) 1700, 1600, 1090, 1060 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.57 (5 H, m), 7.39 (1 H, d, $J$ = 15.0 Hz), 6.95 (1 H, d, $J$ = 15.0 Hz), 2.33 (3 H, s).

**General Procedure for Addition–Elimination Reaction of 1.** A mixture of **1** and excess of the appropriate five-membered heterocycles was stirred in the presence of a catalytic amount of *p*-toluenesulfonic acid (*p*-TsOH) at room temperature for the given period. After addition of aqueous $NaHCO_3$ solution, the product was extracted with ether, washed with brine, dried over $Na_2SO_4$, evaporated in vacuo, and chromatographed on silica gel (*n*-hexane/ethyl acetate) to give the product **3**. The reaction conditions and results are summarized in Table I. The spectroscopic data of products are given in Table II.

**Reaction of *trans*-4-(Phenylsulfonyl)-3-buten-2-one (4) with *N*-Methylpyrrole.** A mixture of **4** (176 mg, 0.83 mmol), *N*-methylpyrrole (1 mL), and a catalytic amount of *p*-TSOH was stirred at room temperature for 10 min and then diluted with ether. The mixture was washed with aqueous $NaHCO_3$ solution, water, and brine, dried over $Na_2SO_4$, and evaporated in vacuo. The residue was chromatographed on silica gel with *n*-hexane/ethyl acetate (2:1) to give 6 (37 mg, 19%) and **5** (180 mg, 74%) in the order of elution. The spectral data of these products are summarized in Table II.

***trans*-(2-Furyl)-3-(2-propynyloxy)-1-butene (7a).** To a stirred solution of **3a** (1.84 g, 13.5 mmol) in methanol (20 mL) at 0 °C was added $NaBH_4$ (1.0 g, 26.4 mmol) in portions and the resulting solution was stirred for 30 min at room temperature. The reaction mixture was diluted with ether, washed with water, dried over $Na_2SO_4$, and evaporated in vacuo to give *trans*-4-(2-furyl)-3-buten-2-ol (1.86 g, 100%) as a pale yellow oil: IR ($CHCl_3$) 3600, 3600–3200 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.34 (1 H, m), 6.47 (1 H, d, $J$ = 16.0 Hz), 6.38 (1 H, m), 6.23 (1 H, m), 6.12 (1 H, d, $J$ = 16.0 Hz), 4.45 (1 H, dq, $J$ = 6.2, 4.8 Hz), 1.74 (1 H, br s, $D_2O$-exchange), 1.35 (3 H, d, $J$ = 6.2 Hz).

This alcohol (1.84 g, 13.3 mmol) was dissolved in a 1:1 mixture (40 mL) of dry benzene and $Me_2SO$ and cooled in an ice bath. To this stirred solution was added dropwise *n*-BuLi in hexane (15.4 mL, 20.0 mmol) and then propargyl bromide (5.4 mL, 60.6 mmol). The resulting mixture was stirred at room temperature for 2.5 h and quenched with aqueous $NH_4Cl$ solution. The organic layers were extracted with ether, washed with brine, dried over $Na_2SO_4$, evaporated, and chromatographed on silica gel with *n*-hexane/ethyl acetate (4:1) to give **7a** (1.37 g, 59%) and the unreacted alcohol (584 mg, 32%) in the order of elution.

Compound **7a**: pale yellow oil; IR (neat) 3280, 2250 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.35 (1 H, d, $J$ = 2.0 Hz), 6.45 (1 H, d, $J$ = 16.0 Hz), 6.37 (1 H, dd, $J$ = 3.0, 2.0 Hz), 6.25 (1 H, d, $J$ = 3.0 Hz), 5.96 (1 H, dd, $J$ = 16.0, 8.0 Hz), 4.21 (1 H, dq, $J$ = 8.0, 6.0 Hz), 4.15 (2 H, dd, $J$ = 16.0, 2.0 Hz), 3.95 (1 H, dd, $J$ = 16.0, 2.0 Hz), 2.40 (1 H, t, $J$ = 2.0 Hz), 1.34 (1 H, d, $J$ = 6.0 Hz); MS, *m*/*e* 176 ($M^+$).

***trans*-1-(*N*-Methyl-2-pyrrolyl)-3-(2-propynyloxy)-1-butene (7b)** was similarly prepared from **3b** in 65–75% overall yield: yellow oil; IR (neat) 3280, 2150 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 6.60 (1 H, d, $J$ = 3.0 Hz), 6.48 (1 H, d, $J$ = 15.9 Hz), 6.37 (1 H, d, $J$ = 2.0 Hz), 6.10 (dd, $J$ = 3.0, 2.0 Hz), 5.78 (1 H, dd, $J$ = 15.9, 7.5 Hz), 4.4–4.0 (3 H, m), 3.63 (3 H, s), 2.40 (1 H, t, $J$ = 2.5 Hz), 1.35 (3 H, d, $J$ = 6.5 Hz); MS, *m*/*e* 189 ($M^+$).

**Intramolecular Diels–Alder Reaction of 7.** A solution of **7a** (1.38 g, 7.9 mmol) in toluene (50 mL) was heated at 150 °C in a sealed tube for 12 h. After cooling, the solvent was evaporated in vacuo, and the residue was chromatographed on silica gel with *n*-hexane/ethyl acetate (20:1) to give **8a** (813 mg, 59%) [$^1H$ NMR ($CDCl_3$) $\delta$ 6.3–6.2 (1 H, m), 6.1–5.9 (1 H, m), 4.6–4.4 (2 H, m), 4.1–3.4 (1 H, m), 2.9–2.3 (3 H, m), 1.35 (3 H, d, $J$ = 6.0 Hz)] which was inseparably contaminated with a certain amount of **9a**. This mixture (314 mg, 1.80 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (410 mg, 1.81 mmol) were dissolved in dry benzene (15 mL) and 2 drops of acetic acid were added. After being stirred at room temperature for 30 min, the mixture was filtered to remove the precipitates, and the filtrate was condensed under the reduced pressure followed by chromatography on silica gel with *n*-hexane/ethyl acetate (10:1) to give 7-methyl-5,7-dihydro-1,6-dioxa-*s*-indacene (**9a**) (225 mg, 72%) as colorless crystals: mp 58–59 °C; IR ($CHCl_3$) 3010, 2980, 2870 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.61 (1 H, d, $J$ = 2.0 Hz, 7.36 (1 H, s), 7.25 (1 H, m), 6.73 (1 H, dd, $J$ = 2.0, 1.0 Hz), 5.38 (1 H, q, $J$ = 6.0 Hz), 5.22 (1 H, dm, $J$ = 11.0 Hz), 5.04 (1 H, dm, $J$ = 11.0 Hz), 1.53 (3 H, d, $J$ = 6.0 Hz); MS, *m*/*e* 174 ($M^+$), 159, 131.

Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 6.37. Found: C, 75.96; H, 6.26.

A similar thermal reaction of **7b** (100 °C, 17 h) afforded a 6:1 mixture of **8a** and **9b** in 38% yield. Compound **8a**: $^1H$ NMR ($CDCl_3$) $\delta$ 6.43 (1 H, d, $J$ = 3.0 Hz), 6.10 (1 H, dd, $J$ = 4.0, 2.0 Hz), 5.95 (1 H, d, $J$ = 3.0 Hz), 4.62 (1 H, dm, $J$ = 14.0 Hz), 4.39 (1 H, dm, $J$ = 14.0 Hz), 3.76 (1 H, dq, $J$ = 8.0, 6.0 Hz), 3.52 (3 H, s), 2.9–2.3 (3 H, m), 1.37 (3 H, d, $J$ = 6.0 Hz). A mixture of **8a**/**9a** (6:1, 80 mg, 0.42 mmol) and 10% Pd/C (10 mg) in ethyl acetate was heated under reflux for 3 h. After filtration of the catalyst and evaporation of the solvent, the residue was chromatographed on silica gel with *n*-hexane/ethyl acetate (10:1) to give 1,7-dimethyl-5,7-dihydrofuro[3,4-*f*]indole (**9b**) (28 mg, 35%) as colorless crystals: mp 88–89 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 7.38 (1 H, s), 7.04 (1 H, s), 7.02 (1 H, d, $J$ = 3.0 Hz), 6.43 (1 H, d, $J$ = 3.0 Hz), 5.40 (1 H, q, $J$ = 6.0 Hz), 5.15 (2 H, m), 3.78 (3 H, s), 1.57 (3 H, d, $J$ = 6.0 Hz); MS, *m*/*e* 187 ($M^+$), 172, 144.

Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48. Found: C, 77.15; H, 7.12; N, 7.60.

**Base-Catalyzed Cyclization of 7.** A solution of **7a** (506 mg, 2.88 mmol) and *t*-BuOK (650 mg, 5.79 mmol) in *t*-BuOH (30 mL) was refluxed under Ar for 1.5 h. After cooling, the reaction mixture was diluted with ether, washed with aqueous $NH_4Cl$ and brine, condensed in vacuo, and chromatographed on silica gel with *n*-hexane/ethyl acetate (10:1) to give 7-methyl-4,7,7a,8-tetrahydro-1,6-dioxa-*s*-indacene (**10a**) (495 mg, 98%) as a colorless oil: IR (neat) 2980, 2930, 2900, 2870 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.28 (1 H, d, $J$ = 2.0 Hz), 6.21 (1 H, d, $J$ = 2.0 Hz), 6.20 (1 H, s), 4.38 (1 H, quintet, $J$ = 6.0 Hz), 3.17 (2 H, small m),

(13) Blum, J.; Pickholts, Y.; Hart, H. *Synthesis* **1972**, 195.

(14) We thank Professor Mitsugi Kozawa of the Osaka College of Pharmacy for a generous supply of a sample of natural psoralen (**11**).

(15) $^1H$ NMR spectroscopy indicates that **20** (mp 180–190 °C dec) exists in solution almost entirely (>95%) in the lactam form.

(16) Matsumura, Y.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1983**, *105*, 6312.

2.10–3.04 (3 H, m), 1.39 (3 H, d, $J$ = 6.0 Hz); MS $m/e$ 176 ($M^+$).

A similar reaction of **7b** afforded 87% of 1,7-dimethyl-4,7,7a,8-tetrahydrofuro[3,4-*f*]indole (**10b**) as a colorless oil: IR (neat) 2960, 2920, 2800 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 6.51 (1 H, d, $J$ = 3.0 Hz), 6.17 (1 H, br s), 5.93 (1 H, d, $J$ = 3.0 Hz), 4.37 (1 H, quintet, $J$ = 6.0 Hz), 3.46 (3 H, s), 3.27 (2 H, small m), 2.2–3.05 (3 H, m) 1.39 (3 H, d, $J$ = 6.0 Hz); MS, $m/e$ 189 ($M^+$), 174.

**Preparation of *trans*-1-(Phenylsulfinyl)-1-hepten-6-yn-3-one (12).** (a) To a stirred solution of LDA (50.6 mmol), prepared from diisopropylamine (5.12 g, 50.6 mmol) and *n*-BuLi (50.6 mmol), in dry THF (50 mL) was added ethyl acetoacetate (3.29 g, 25.3 mmol) in THF (20 mL) at 0 °C. After 30 min, propargyl bromide (2.25 mL, 25.3 mmol) was added in one portion and the resulting solution was stirred for additional 1 h at 0 °C followed by addition of acetic acid (2.90 mL, 50.6 mmol), ether, and water. The organic layers were extracted with ether, washed with brine, dried over $Na_2SO_4$, condensed in vacuo, and distilled on Kugelrohr (90–100 °C/3 mmHg) to give ethyl 3-oxo-6-heptynoate (2.97 g, 70%) as a colorless oil: IR (neat) 1760–1710 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.21 (2 H, q, $J$ = 7.0 Hz), 3.47 (2 H, s), 3.0–2.3 (4 H, m), 1.96 (1 H, t, $J$ = 2.2 Hz), 1.28 (3 H, t, $J$ = 7.0 Hz).

(b) The above keto ester (2.96 g, 17.6 mmol) was ketalized in the usual way to give ethyl 2-[2-(3-butynyl)-1,3-dioxolan-2-yl]acetate (3.68 g, 99%) as pale yellow oil: IR (neat) 1740 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.16 (2 H, q, $J$ = 7.2 Hz), 3.99 (4 H, s), 2.66 (2 H, s), 2.3–2.0 (4 H, m), 1.93 (1 H, t, $J$ = 2.2 Hz), 1.27 (3 H, q, $J$ = 7.2 Hz).

(c) To a stirred suspension of $LiAlH_4$ (1.92 g, 50.5 mmol) in dry ether (300 mL) at 0 °C was added an ethereal solution of the above ketal (11.0 g, 50.5 mmol). After stirring for 30 min at room temperature, the usual workup afforded 2-(3-butynyl)-2-(2-hydroxyethyl)-1,3-dioxolane (8.53 g, 99%) as a colorless oil: IR (neat) 3600–3200 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.01 (4 H, s), 3.76 (2 H, q, $J$ = 5.4 Hz), 2.60 (1 H, t, $J$ = 5.4 Hz), 2.5–1.8 (7 H, m).

(d) To a stirred solution of the above alcohol (2.77 g, 16.3 mmol) in benzene (10 mL) was added dropwise tri-*n*-butylphosphine (6.08 mL, 24.4 mmol). After being stirred for 30 min, the reaction mixture was diluted with ether, washed with aqueous 5% NaOH and water, and evaporated in vacuo. Chromatography of the residue on silica gel with *n*-hexane/ethyl acetate (4:1) gave 2-(3-butynyl)-2-[2-(phenylthio)-ethyl]-1,3-dioxolane (4.27 g, 100%) as a colorless oil: $^1H$ NMR ($CDCl_3$) $\delta$ 7.28 (5 H, m), 3.95 (4 H, s), 3.2–2.7 (2 H, m), 2.5–1.6 (7 H, m).

(e) A solution of the above sulfide (12.5 g, 47.6 mmol) and concentrated HCl (120 mL) in THF (200 mL) was stirred at 0 °C for 20 min, and the usual workup gave 1-(phenylthio)-6-heptyn-3-one (10.2 g, 98%) as a pale yellow oil: IR (neat) 1720 $cm^{-1}$; $^1H$ NMr ($CDCl_3$) $\delta$ 7.29 (5 H, m), 3.3–2.9 (2 H, m), 2.9–2.3 (2 H, m), 2.5–2.2 (4 H, m), 1.94 (1 H, t, $J$ = 2.2 Hz).

(f) A mixture of the above ketone (10.2 g, 46.7 mmol) and *N*-chlorosuccinimide (8.11 g, 60.7 mmol) in benzene (120 mL) was stirred for 4 h at 0 °C and then 10 min at room temperature. After cooling again to 0 °C, triethylamine (19.5 mL, 140 mmol) was added and the mixture was stirred for further 3 h at 0 °C to room temperature. The usual workup and chromatography on silica gel (*n*-hexane/ethyl acetate = 15:1) gave an $E/Z$ mixture of 1-(phenylthio)-6-hept-1-en-6-yn-3-one (6.4 g, 63%): IR (neat) 1680, 1665 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.79 (1 H, d, $J$ = 15.4 Hz, *E* isomer), 7.44 (5 H, m), 6.38 (1 H, d, $J$ = 9.6 Hz, *Z* isomer), 6.04 (1 H, d, $J$ = 15.4 Hz, *E* isomer), 2.9–2.2 (4 H, m), 1.94 (1 H, t, $J$ = 2.0 Hz).

(g) To a stirred solution of the above ketone (2.95 g, 13.6 mmol) in $CH_2Cl_2$ (50 mL) was added dropwise at 0 °C a solution of 80% *m*-CPBA (2.05 g, 9.52 mmol) in $CH_2Cl_2$ (40 mL), and the resulting mixture was stirred for further 30 min at room temperature. The usual workup and chromatography on silica gel (*n*-hexane/ethyl acetate = 1:1) afforded the unreacted ketone (670 mg, 23%) and **12** (2.01 g, 64%) as colorless crystals: mp 83–84 °C; IR ($CHCl_3$) 3300, 3000, 2155, 1705, 1600, 1090, 1060 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.59 (5 H, m), 7.46 (1 H, d, $J$ = 15.0 Hz), 6.99 (1 H, d, $J$ = 15.0 Hz), 3.1–2.7 (2 H, m), 2.7–2.3 (2 H, m), 1.95 (1 H, t, $J$ = 2.2 Hz); MS, $m/e$ 232 ($M^+$).

***trans*-1-(2-Furyl)-1-hepten-6-yn-3-one (13).** A mixture of **12** (1.41 g, 6.08 mmol) and *p*-TsOH (50 mg) in furan (10 mL) was stirred at room temperature for 7 h. The reaction mixture was diluted with ether, washed with aqueous $NaHCO_3$ and brine, dried over $Na_2SO_4$, and chromatographed on silica gel (*n*-hexane/ethyl acetate = 15:1) to give **13** (825 mg, 78%) as a pale yellow oil: IR ($CHCl_3$) 3290, 3000, 2160, 1690, 1660 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.51 (1 H, br s), 7.38 (1 H, d, $J$ = 15.6 Hz), 6.69 (1 H, d, $J$ = 3.6 Hz), 6.63 (1 H, d, $J$ = 15.6 Hz), 6.5 (1 H, m), 3.1–2.7 (2 H, m), 2.7–2.3 (2 H, m), 1.97 (1 H, t, $J$ = 2.4 Hz); MS, $m/e$ 174 ($M^+$).

**2-(3-Butynyl)-5,5-dimethyl-2-[*trans*-2-(2-furyl)vinyl]-1,3-dioxane (14).** A solution of **13** (278 mg, 1.60 mmol), neopentyl glycol (330 mg, 3.17 mmol), and *p*-TsOH (15 mg) in dry benzene was azeotropically refluxed for 1 h. After being cooled to room temperature, the reaction mixture was diluted with ether and aqueous $NaHCO_3$. The usual workup and chromatography on silica gel (*n*-hexane/ethyl acetate = 10:1) gave **14** (307 mg, 74%) as a colorless oil and the unreacted **13** (56 mg, 20%) in the order of elution.

Compound **14**: IR (neat) 3290, 2160 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.36 (1 H, d, $J$ = 1.8 Hz), 6.46 (1 H, d, $J$ = 16.0 Hz), 6.39 (1 H, m), 6.28 (1 H, d, $J$ = 3.5 Hz), 5.97 (1 H, d, $J$ = 16.0 Hz), 3.63 (1 H, d, $J$ = 10.5 Hz), 3.33 (1 H, d, $J$ = 10.5 Hz) , 2.6–2.3 (2 H, m), 2.1–1.8 (3 H, m), 1.16 (3 H, s), 0.68 (3 H, s).

**Thermal Reaction of 14.** (a) A solution of **14** (280 mg, 1.08 mmol) in toluene (3 mL) was heated at 200 °C under Ar in a sealed tube for 12 h. After cooling, the reaction mixture was condensed in vacuo and chromatographed on silica gel with *n*-hexane/ethyl acetate (20:1) to give **16** (8 mg, 3%) and **15** (160 mg, 57%) in the order of elution.

**Compound 15**: pale yellow oil; IR ($CHCl_3$) 3000, 2940, 2850, 1470 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.56 (1 H, d, $J$ = 2.7 Hz), 7.39 (1 H, d, $J$ = 8.7 Hz), 7.38 (1 H, d, $J$ = 1.5 Hz), 7.10 (1 H, dd, $J$ = 8.7, 1.5 Hz), 6.69 (1 H, m), 4.40 (1 H, t, $J$ = 5.5 Hz), 3.61 (1 H, d, $J$ = 11.0 Hz), 3.39 (1 H, d, $J$ = 11.0 Hz), 2.83 (1 H, dd, $J$ = 8.0, 7.0 Hz), 2.00 (1 H, ddd, $J$ = 8.0, 7.0, 5.5 Hz), 1.21 (3 H, s), 0.71 (3 H, s); MS, $m/e$ 260 ($M^+$).

**Compound 16**: pale yellow oil; IR (neat) 2940, 2860, 1740, 1470 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.60 (1 H, d, $J$ = 2.1 Hz), 7.43 (1 H, m), 7.43 (1 H, d, $J$ = 8.5 Hz), 7.13 (1 H, dm, $J$ = 8.5 Hz), 3.77 (2 H, s), 3.3–2.9 (2 H, m), 2.9–2.5 (2 H, m), 0.90 (9 H, s).

(b) A mixture of **14** (284 mg, 1.09 mmol) and 10% Pd/C (110 mg) in xylene (10 mL) was vigorously stirred at 200 °C under Ar in a sealed tube for 19 h. The mixture was filtered, evaporated, and chromatographed on silica gel (*n*-hexane/ethyl acetate = 20:1) to give **15** (43 mg, 15%), **16** (43 mg, 15%), and **17** (107 mg, 38%) as a pale yellow oil: IR ($CHCl_3$) 2950, 2860, 1450 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.65 (1 H, m), 7.62 (1 H, d, $J$ = 2.4 Hz), 7.40 (1 H, s), 6.70 (1 H, dd, $J$ = 2.4, 1.0 Hz), 3.82 (2 H, dm, $J$ = 11.0 Hz), 3.57 (2 H, dm, $J$ = 11.0 Hz), 3.2–2.8 (2 H, m), 2.7–2.3 (2 H, m), 1.39 (3 H, s), 0.87 (3 H, s).

**5,6-Dihydro-1-oxa-*s*-indacen-7-one (18).** A solution of **17** (110 mg, 0.43 mmol) and 10% HCl (5 mL) in THF (10 mL) was stirred at room temperature for 1.5 h. The reaction mixture was diluted with ether, washed with water and aqueous $NaHCO_3$, dried over $Na_2SO_4$, and chromatographed on silica gel (*n*-hexane/ethyl acetate = 4:1) to give **18** (73 mg, 100%) as colorless crystals: mp 146–147 °C ($CHCl_3$/*n*-hexane); IR ($CHCl_3$) 3000, 2930, 1705, 1620, 1470, 1440 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.87 (1 H, s), 7.78 (1 H, d, $J$ = 2.0 Hz), 7.63 (1 H, s), 6.81 (1 H, dm, $J$ = 2.0 Hz), 3.4–3.1 (2 H, m), 2.9–2.6 (2 H, m); MS, $m/e$ 172 ($M^+$), 144.

Anal. Calcd for $C_{11}H_8O_2$: C, 76.73; H, 4.68. Found: C, 76.88; H, 4.72.

**Psoralen (11).** (a) Baeyer–Villiger oxidation of **18** was performed by the method of Hart et al.[13] To a mixture of acetic anhydride (5 mL) and concentrated $H_2SO_4$ (1.25 mL) was added dropwise 30% hydrogen peroxide (1.25 mL) with vigorous stirring at −10 °C. The mixture was dissolved in $CH_2Cl_2$ (4 mL) and added to a stirred solution of **18** (250 mg, 1.45 mmol) in $CH_2Cl_2$ (10 mL). After being stirred at room temperature for 30 min, the mixture was diluted with $CH_2Cl_2$, washed with water and aqueous $NaHCO_3$, evaporated, and chromatographed on silica gel ($CHCl_3$) to give 3,4-dihydropsoralen (195 mg, 71%) as a colorless solid: mp 98–101 °C; IR ($CHCl_3$) 1780, 1760, 1460 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.62 (1 H, d, $J$ = 2.3 Hz), 7.38 (1 H, s), 7.23 (1 H, s), 6.72 (1 H, dd, $J$ = 2.3, 1.2 Hz), 3.2–2.9 (2 H, m), 2.9–2.6 (2 H, m); MS, $m/e$ 188 ($M^+$), 160, 146.

(b) A mixture of 3,4-dihydropsoralen (120 mg, 0.64 mmol) and 10% Pd/C (100 mg) in diphenyl ether (1.5 mL) was heated under reflux for 8 h. After filtration through a Celite column, the filtrate was chromatographed on silica gel with first *n*-hexane to give diphenyl ether and then with n-hexane/ethyl acetate (4:1) to give **11** (46 mg, 39%) as colorless crystals: mp 160–161 °C (ether) (lit.[3] mp 161–162 °C); IR ($CHCl_3$) 1735, 1640, 1580 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.80 (1 H, d, $J$ = 9.5 Hz), 7.70 (1 H, d, $J$ = 2.2 Hz), 7.69 (1 H, s), 7.48 (1 H, m), 6.84 (1 H, dd, $J$ = 2.2, 1.0 Hz), 6.38 (1 H, d, $J$ = 9.5 Hz); MS, $m/e$ 186 ($M^+$), 158; high-resolution MS, $m/e$ ($M^+$) calcd for $C_{11}H_6O_3$, 186.0317; found, 186.0292.

**11** was identical with a sample of the natural psoralen[14] in all respects (TLC, IR, NMR, MS).

**5,6-Dihydro-1-oxa-*s*-indacen-7-one Oxime (19).** To a solution of hydroxylamine hydrochloride (84 mg, 1.2 mmol) and sodium acetate (244 mg, 1.8 mmol) in water (2 mL) was added an ethanol solution (10 mL) of **18** (102 mg, 0.60 mmol), and the resulting mixture was heated under reflux for 4 h. The mixture was diluted with ether, washed with water, and dried over $Na_2SO_4$. The evaporation of the solvent under the reduced pressure gave **19** (111 mg, 98%) as colorless solid which was recrystal-

lized from ethanol: mp 210 °C (sublim); IR (KBr) 3600-2800, 2920, 1620, 1440 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 13.6-11.6 (1 H, br s, $D_2O$-exchange), 7.77 (1 H, s), 7.67 (1 H, d, $J$ = 1.8 Hz), 7.49 (1 H, s), 6.74 (1 H, m), 3.10 (4 H, s); MS, $m/e$ 187 ($M^+$).

**2-Oxo-1,2-dihydrofuro[3,2-*g*]quinoline (20).** (a) To a stirred solution of **19** (37 mg, 0.20 mmol) and triethylamine (0.05 mL, 0.38 mmol) in dry $CH_2Cl_2$ (2 mL) was added dropwise at 0 °C methanesulfonyl chloride (0.02 mL, 0.3 mmol). The resulting mixture was stirred for 20 min at this temperature, diluted with ether, washed with 10% HCl and brine, dried over $Na_2SO_4$, and condensed under the reduced pressure to give 7-(methanesulfonyloxyimino)-6,7-dihydro-5*H*-1-oxa-*s*-indacene (46 mg, 100%) as a solid which was recrystallized from ethyl acetate/*n*-hexane to give colorless crystals: mp 130 °C dec; $^1H$ NMR ($CDCl_3$) $\delta$ 7.91 (1 H, s), 7.74 (1 H, d, $J$ = 2.2 Hz), 7.55, (1 H, s), 6.79 (1 H, m), 3.26 (3 H, s), 3.19 (4 H, s).

(b) Beckmann rearrangement was performed by the modified method of Yamamoto et al.[16] To a solution of the above mesylate (35 mg, 0.15 mmol) in $CH_2Cl_2$ was added at −70 °C a 15% hexane solution of diethylaluminum chloride (0.55 mL, 0.45 mmol) and the resulting solution was stirred for 30 min at this temperature. After being warmed up to room temperature, the mixture was stirred for further 1 h and quenched with aqueous 5% NaOH solution (3 mL). Extraction with $CH_2Cl_2$ and evaporation of the solvent gave **21** as a solid (18 mg, 65%) which was recrystallized from ether to give yellow crystals: mp 214-217 °C; IR ($CHCl_3$) 3400, 3000, 1685, 1640 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.8-8.4 (1 H, br s), 7.55 (1 H, d, $J$ = 2.0 Hz), 7.37 (1 H, s), 6.99 (1 H, s), 6.69 (1 H, m), 3.3-2.9 (2 H, m), 2.8-2.5 (2 H, m); MS, $m/e$ 187 ($M^+$), 159.

(c) A mixture of the above lactam (30 mg, 0.16 mmol) and 10% Pd/C (30 mg) in diphenyl ether (1 mL) was refluxed for 4 h under Ar. The workup as described above and chromatography on silica gel (*n*-hexane/ethyl acetate = 4:1) afforded **20** (9 mg, 28%) as colorless crystals: mp 180-190 °C dec; IR ($CHCl_3$) 1665 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.0-7.4 (1 H, br s), 7.90 (1 H, d, $J$ = 9.5 Hz), 7.78 (1 H, s), 7.66 (1 H, d, $J$ = 2.2 Hz), 7.48 (1 H, m), 6.82 (1 H, dd, $J$ = 2.2, 1.0 Hz), 6.67 (1 H, d, $J$ = 9.5 Hz); high-resolution MS, $m/e$ ($M^+$) calcd for $C_{11}H_7NO_2$, 185.0476; found: 185.0450.

**1-Oxo-1,2,3,4-tetrahydrofuro[3,2-*g*]isoquinoline (22).** A mixture of **19** (37 mg, 0.20 mmol) and polyphosphoric acid (PPA) (1 g) was heated at 90 °C for 3 h. After addition of water, the product was extracted with ether, and the organic phases were washed with aqueous $NaHCO_3$ and brine and dried over $Na_2SO_4$. Evaporation of the solvent in vacuo gave **22** (21 mg, 57%) as a colorless solid: IR ($CHCl_3$) 3410, 2920, 1670 $cm^{-1}$; $^1H$ NMR $\delta$ 8.27 (1 H, s), 7.74 (1 H, d, $J$ = 2.2 Hz), 7.43 (1 H, s,), 6.76 (1 H, m), 6.2-5.8 (1 H, br s), 3.8-3.4 (2 H, m), 3.2-2.8 (2 H, m).

**Registry No. 1**, 91798-67-3; **3a**, 41438-24-8; **3b**, 2433-64-9; **3c**, 66434-99-9; **3d**, 2433-57-0; **3e**, 91798-68-4; **3f**, 91164-84-0; **3g**, 91798-69-5; **4**, 21860-46-8; **5**, 91798-70-8; **6**, 91798-71-9; **7a**, 91798-72-0; **7b**, 91798-73-1; **8a**, 91798-74-2; **8b**, 91798-75-3; **9a**, 91798-76-4; **9b**, 91798-77-5; **10a**, 91798-78-6; **10b**, 91798-79-7; **11**, 66-97-7; **12**, 91798-80-0; **13**, 91798-81-1; **14**, 91798-82-2; **15**, 91798-83-3; **16**, 91798-84-4; **17**, 91798-85-5; **18**, 91798-86-6; **19**, 91798-87-7; **20**, 91798-88-8; **21**, 91798-89-9; **22**, 91798-90-2; (*E*)-PhSCH=CHC(O)$CH_3$, 33944-98-8; (*Z*)-PhSCH=CHC(O)$CH_3$, 33944-97-7; CH≡$CCH_2$Br, 106-96-7; $CH_3C(O)CH_2C(O)OEt$, 141-97-9; CH≡$C(CH_2)_2C(O)CH_2C(O)OEt$, 35116-07-5; CH≡$C(CH_2)_2C(O)(CH_2)_2SPh$, 91798-94-6; (*E*)-PhSCH=CHC(O)$(CH_2)_2C$≡CH, 91798-95-7; (*Z*)-PhSCH=CHC(O)$(CH_2)_2C$≡CH, 91798-96-8; furan, 110-009; 2-methylfuran, 534-22-5; 1*H*-pyrrole, 109-97-7; 1-methyl-1*H*-pyrrole, 96-54-8; 1*H*-pyrazole, 288-13-1; 1*H*-imidazole, 288-32-4; 6-(dimethylamino)fulvene, 696-68-4; *trans*-4-(2-furyl)-3-buten-2-ol, 79380-04-4; ethyl 2-[2-(3-butynyl)-1,3-dioxolan-2-yl]acetate, 91798-91-3; 2-(3-butynyl)-2-(2-hydroxyethyl)-1,3-dioxolane, 91798-92-4; 2-(3-butynyl)-2-[2-(phenylthio)ethyl]-1,3-dioxolane, 91798-93-5; neopentyl glycol, 126-30-7; 3,4-dihydropsoralen, 6544-89-4; 7-[[(methylsulfonyl)oxy]imino]-6,7-dihydro-5*H*-1-oxa-*s*-indacene, 91798-97-9.

# Autoxidation and Aggregation of Phospholipids in Organic Solvents

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**Abstract:** The $^{31}$NMR $Pr^{3+}$ shift reagent method indicates that phospholipids, dipalmitoylphosphatidylcholine (DPPC), dilinoleoylphosphatidylcholine (DLPC), and egg lecithin (ELPC) aggregate in organic solvents benzene, chlorobenzene, and *o*-dichlorobenzene to form reverse micelles with aggregation numbers in the range 80-100 when the water/phospholipid mole ratio is 20/1. In the presence of lower water/phospholipid ratios (ca. 2 to 16) in these solvents, the $^{31}$P NMR method used with both inorganic, $Pr^{3+}$, and organic-soluble shift reagent $Pr(DPM)_3$ indicates the presence of both monomers and aggregates, the latter increasing regularly with the water content. Sedimentation results on ELPC in *o*-dichlorobenzene show the presence of aggregates in the absence of added water. There was no evidence for aggregation of a phospholipid in the protic solvent *tert*-butyl alcohol ($^{31}$P method). Product studies of conjugated hydroperoxides from autoxidation of DLPC and 1-palmitoyl-2-linoleoylphosphatidylcholine (1P-2LPC) in organic solvents, compared to these products from methyl linoleate and linoleic acid, indicate that these phospholipids aggregate in organic solvents and this influences the kinetics and product distribution of autoxidation. The kinetics of autoxidation of ELPC and DLPC thermally initiated with di-*tert*-butyl hyponitrite in organic solvents are studied. The rates of photochemically initiated autoxidation of DLPC in organic solvents are accelerated by added water. The increased rate is shown to be related to the fraction of phospholipid aggregated into reverse micelles. The oxidizability of an unsaturated phospholipid (DLPC) in reverse micelles is estimated to be 2 or 3 times higher than that of a homogeneously dispersed substrate. The oxidizability of DLPC in a bilayer is similar to that in *homogeneous* solution.

Lipid peroxidation, the uncontrolled reaction of lipids and molecular oxygen, is a threat to aerobic organisms. The autoxidation of polyunsaturated fatty acids present in phospholipids that make up biomembranes affects cell structure and function, for example, through increased cell membrane permeability.[1]

Recognition of the significance of lipid peroxidation to important pathological events has attracted increased interest in the autoxidation of biologically important molecules[2-4] and the study of

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