Ring Construction Using 3-(Arylmethylene)-2,4(3*H*,5*H*)-furandione: Synthesis of Pyrazolones and Furo[3,4-*c*][1,5]benzothiazepinones[1-3]

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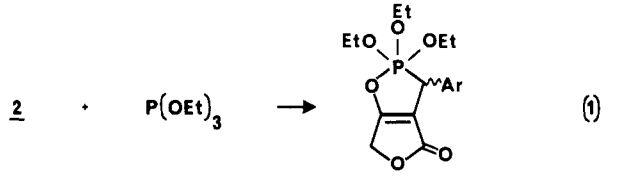
The ring transformation of 3-(arylmethylene)-2,4(3*H*,5*H*)-furandiones (**2**) into the corresponding pyrazolones (**3**) is described. The conversion with selected hydrazines proceeds regioselectively to form a uniquely substituted pyrazolone system (**3**) as the major product. With 2-aminothiophenol, **2** reacts to form a novel fused heterocyclic array, the furo[3,4-*c*][1,5]benzothiazepinone ring system. Details of this heteroannelation are presented.

In continuation of our interest in the chemical versatility of 2,4(3*H*-5*H*)-furandione (β-tetronic acid, **1**) and 3-(arylmethylene)-2,4(3*H*,5*H*)-furandiones[1a,2,4] **2**, we determined that **1** and **2** represent easily accessable building blocks for the synthesis of heterocyclic systems. In **1** the active methylene carbon is a nucleophilic site, while the ketone and ester carbonyls represent electrophilic sites. These can be used to advantage for annelations to form fused heterocyclic systems.[1b] By reacting **1** with an annelating reactant that contains complementary electrophilic and nucleophilic sites for bond formation and ring closure, condensed heterocyclic systems can be obtained.[1b,2,4,5] While this mode of reaction is not possible in **2**, we showed, however, that triethyl phosphite adds in a Michael fashion to yield the novel 2,5-dihydrofuro[3,4-*d*]-1,2-oxaphosphin-4(6*H*)-one ring system[4] (eq. 1).



(1)

In this report we describe two ring forming reactions utilizing **2**. The first one is a ring transformation and involves the reaction of **2** with selected hydrazines to give substituted pyrazolones **3**. The second is a heteroannelation reaction and deals with the product of the interaction between **2** and 2-aminothiophenol to form the unique furo[3,4-*c*][1,5]benzothiazepinone ring system.

Results and Discussion

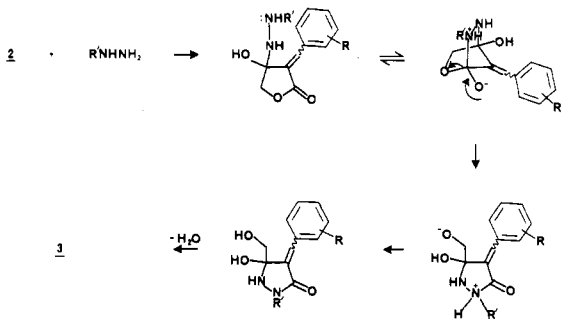
Reaction between Compounds 2 and Hydrazines. Earlier, Wolff[6] reported that **1** reacts with phenylhydrazine to give the expected hydrazone. More recently, Gelin and co-workers investigated the reaction of a number of substituted **1** with a variety of hydrazines and reported formation of the 1,2,3-triazolo and furazan systems,[7] the pyrazole system,[8,9] and the condensed 6*H*-furo[1,3-*c*]-pyrazole and the pyrrolo[3,4-c]pyrazole systems.[10]

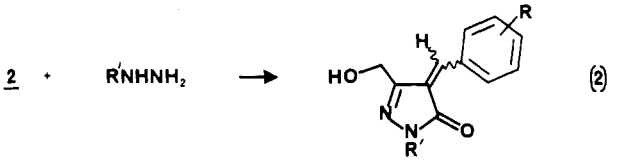
In the light of these findings[6-10] and our results,[4] we decided to investigate the reaction between type **2** compounds[2-4] and hydrazine. It was found that the reaction of 1 equiv of hydrazine hydrate with type **2** compounds proceeds regioselectively to give crystalline 2,4-dihydro-5-(hydroxymethyl)-4-(arylmethylene)-3*H*-pyrazol-3-ones **3** (eq 2, Table I). Similarly, when methylhydrazine was used, the corresponding *N*-methylpyrazol-3-ones were obtained (eq 2, Table I). Thus, **2** reacts as a β-keto ester

Table I. Pyrazolones 3 from 3-(Arylmethylene)-2,4-(3*H*,5*H*)-furandiones (2)

no.	R	R′	yield, %
3a	3,4-methylenedioxy	H	79
3b	3,4,5-trimethoxy	H	58
3c	4-chloro	H	51
3d	2-chloro	H	65
3e	H	H	56
3f	2-nitro	H	48
3g	3,4-methylenedioxy	CH_3	74
3h	3,4-dimethoxy	CH_3	75
3i	3,4,5-trimethoxy	CH_3	46
3j	4-chloro	CH_3	44
3k	H	CH_3	51

Scheme I





(2)

where R′ = H or CH_3 **3**

(1) (a) This is part 33 of the series: Substituted γ-Butyrolactones. (b) For part 32 of this series see: Schmidt, D. G.; Zimmer, H. *J. Heterocycl. Chem.* **1983**, *20*, 787.

(2) Abstracted in part from the Ph.D. Dissertation of D. G. Schmidt, University of Cincinnati, 1981.

(3) Presented at the 181st National Meeting of the American Chemical Society Atlanta, GA; April 1981; ORGN 172.

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(9) Chantegrel, B.; Gelin, S. *Synthesis* **1979**, 584.

(10) Gelin, S.; Chantegrel, B.; Chabannet, M. *Synth. Commun.* **1982**, *12*, 431.

0022-3263/83/1948-4367$01.50/0

Table II. 10-Aryl-4,10-Dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-ones (5) from 2

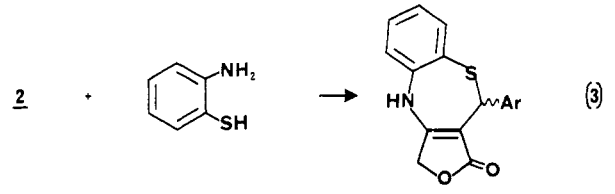
no.	Ar	yield, %
5a	3,4-methylenedioxyphenyl	74 (53)[a]
5b	3,4-dimethoxyphenyl	71
5c	3,4,5-trimethoxyphenyl	60
5d	4-chlorophenyl	84 (54)[a]
5e	2-chlorophenyl	88
5f	4-bromophenyl	74
5g	phenyl	78 (26)[a]
5h	2-nitrophenyl	98
5i	5-methyl-2-thienyl	79

[a] Yield obtained without added acid.

with the hydrazines studied, as opposed to behaving as an α,β-unsaturated ketone or ester. While TLC revealed the formation of other products, none of these appeared to be major. No attempt to isolate and characterize them was made. Scheme I outlines a plausible mechanism for the formation of **3**.

Thus, the reaction of **2** with hydrazines affords a convenient route to the pyrazolones **3**. The structural assignment of **3** is based upon confirming ^{1}H NMR, IR, mass spectral, and combustion analysis data. ^{1}H NMR features exhibited by type **3** compounds included for **3a–f** the respective phenyl ring proton resonances; the $-CH_2OH$ group, fortuitously resonating as a singlet over the range of 4.95–5.03 ppm; the vinyl proton occurring between 7.88 and 8.42 ppm; and the exchangeable NH proton at 11.23–11.83 ppm. Proton resonances observed for **3g-k** included, in addition to the phenyl ring proton resonances, the $-CH_2OH$ group appearing as two closely spaced apparent singlets between 5.07 and 5.3 ppm; the vinyl proton resonating over the range of 7.93–8.2 ppm; and the *N*-methyl moiety at 3.33-3.67 ppm.

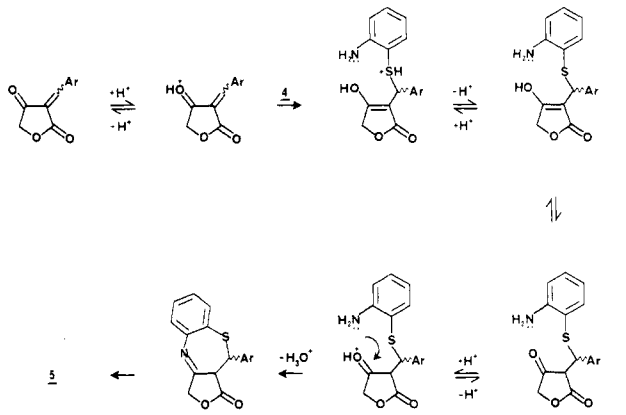
Reaction between Compounds 2 and 2-Aminothiophenol. In the preceding section it was shown that type 2 compounds react with hydrazine and methylhydrazine as β-keto esters. In contrast, the reaction of type 2 compounds[2] with 2-aminothiophenol (**4**) proceeds quite differently. Here, they behave as α,β-unsaturated ketones to yield the novel furo[3,4-*c*][1,5]benzothiazepinone system **5** (eq 3).



When 1 equiv of a type **2** compound in absolute ethanol and 1 equiv of **4** are refluxed together for 1 h, type **5** compounds are obtained directly in a single operation. While the condensation occurs in the absence of acid, yields are greatly improved when an equivalent of concentrated hydrochloric acid is added (Table II).

We propose the mechanism shown in Scheme II for the formation of **5**. The addition of acid causes the ketone carbonyl group to be protonated. This renders the already electron-poor α,β-carbon–carbon double bond even more electron deficient. Nucleophilic attack by sulfur at the β-carbon followed by proton loss gives the thioether shown. Ketonization followed by protonation of the ketone group facilitates Schiff base formation. Loss of H_3O^+ and tautomerization affords **5**. This proposed mechanism is consistent with the greater nucleophilicity of SH relative

Scheme II



to NH_2 as shown for the reaction between chalcones and **4**.[11]

The generality of this reaction is illustrated by the good to excellent yields obtained with a variety of electron-withdrawing and electron-releasing substituents on the phenyl group of **2**. Further, when **2** has a heteroaromatic ring in place of a phenyl ring, the reaction also occurs smoothly and in high yield (Table II).

The structure of type **5** compounds were assigned on the basis of elemental analysis, mass spectra, IR, and ^{1}H NMR data. The ^{1}H NMR and mass spectral data for **5** show certain common features. Accompanying the phenyl ring proton resonances, ^{1}H NMR signals characteristically exhibited by **5** at 60 MHz were a singlet for the lactone methylene protons at ~5.0 ppm; a singlet for the benzylic proton occurring over the range of 5.27–6.03 ppm, depending on the substituents on the phenyl ring; and the exchangeable N–H proton measured at 10.17–10.38 ppm. Electron-impact mass spectra of **5** gave specific fragmentation features including the molecular ion peak and loss of the substituted phenyl group at position 10 and M – 59. This latter peak was frequently of highest intensity. Deuterium exchange and *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) derivatization further confirmed the presence of only one exchangeable proton.

Conclusions. Ring transformations of heterocyclic systems are an important area of chemistry from both theoretical as well as practical view points.[12] The regioselective synthesis of the uniquely substituted pyrazolones **3** by treatment of **2** with hydrazines, as presented here, occurs readily. This ring interconversion represents a convenient route to an otherwise difficultly accessable substituted pyrazolone.

The functionality in **2** has been further utilized to form the novel furo[3,4-*c*][1,5]benzothiazepinone ring system **5** by heteroannelation with 2-aminothiophenol. This new fused array is readily available in high yield by this route.

In summary, the furandione **2** has been demonstrated to be a versatile, multifunctional, synthetic building block for the construction of novel, substituted heterocyclic systems.

Experimental Section

Infrared spectra (IR) were obtained on a Perkin-Elmer Model 599 spectrometer and were calibrated against the 1601-cm^{-1} band of polystyrene. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Varian T-60 spectrometer. Chemical

(11) Toth, G.; Szöllösy, A.; Levai, A.; Duddeck, H. *Org. Magn. Reson.* **1982**, *20*, 133.

(12) Van der Plas, H. C. "Ring Transformations of Heterocycles"; Academic Press: New York and London, 1973; Vol. I and II.

shifts are reported on the δ scale in parts per million downfield from internal tetramethylsilane (Me_4Si), and apparent coupling constants (J) are given in hertz (Hz). Carbon-13 nuclear magnetic resonance data (^{13}C NMR) were obtained on a Bruker HFX-90 instrument with Me_4Si as the internal standard. A Perkin-Elmer RMU-7 mass spectrometer was used to record mass spectral data at 70 eV. Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, or by M-H-W Laboratories, Phoenix, AZ.

Preparation of 4-(Arylmethylene)-2,4-dihydro-5-(hydroxymethyl)-3*H*-pyrazol-3-ones 3a–f and 4-(Arylmethylene)-2,4-dihydro-5-(hydroxymethyl)-2-methyl-3*H*-pyrazol-3-ones 3g–k. General Method. To the appropriate 3-(arylmethylene)-2,4(3*H*,5*H*)-furandione **2** (2 mmol) in absolute ethanol (2 mL) was added hydrazine (1 mL, 2 M ethanolic hydrazine) or methylhydrazine (1 mL, 2 M ethanolic methylhydrazine) where appropriate. The resulting solution was refluxed for 1 h, during which time a precipitate formed. The reaction mixture was chilled in an ice–water bath and was filtered. The precipitate was washed with cold ethanol then dried in vacuo in the presence of P_4O_{10}. Analytical samples were recrystallized from acetonitrile. The following compounds were prepared in this manner.

4-[(1,3-Benzodioxol-5-yl)methylene]-2,4-dihydro-5-(hydroxymethyl)-3*H*-pyrazol-3-one (3a): mp 260–260.5 °C; ^1H NMR (Me_2SO-d_6) δ 4.95 (s, 3 H, 1 of 3 NaOD/D_2O exchangeable) 6.05 (s, 2 H), 6.82–7.35 (m, 3 H), 7.88 (s, 1 H), 11.35 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3460, 3130, and 3070 (OH, NH), 1725 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 246 (M^+, 100). Anal. Calcd for $C_{12}H_{10}N_2O_4$: C, 58.53; H, 4.09; N, 11.38. Found: C, 58.63; H, 4.14; N, 11.15.

4-[(3,4,5-Trimethoxyphenyl)methylene]-2,4-dihydro-5-(hydroxymethyl)-3*H*-pyrazol-3-one (3b): mp 179–180 °C; ^1H NMR (Me_2SO-d_6) δ 3.37 (s, 3 H), 3.48 (s, 6 H), 4.98 (br s, 3 H, 1 of 3 NaOD/D_2O exchangeable), 7.02 (s, 2 H), 7.93 (s, 1 H), 11.5 (br s, 1 H); IR (KBr) 3440 and 2940 (OH, NH), 1720 (C=O); mass spectrum, m/e (relative intensity) 292 (M^+, 100). Anal. Calcd for $C_{14}H_{16}N_2O_5$: C, 57.53; H, 5.52; N, 9.59. Found: C, 57.73; H, 5.56; N, 9.49.

4-[(4-Chlorophenyl)methylene]-2,4-dihydro-5-(hydroxymethyl)-3*H*-pyrazol-3-one (3c): mp 214–215 °C; ^1H NMR (Me_2SO-d_6) δ 5.02 (s, 3 H, 1 of 3 NaOD/D_2O exchangeable), 7.38–7.93 (A_2B_2 pattern, 4 H), 8.05 (s, 1 H), 11.63 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3450, 3120, and 3050 (OH, NH), 1735 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 236 (M^+, 35), 238 (M^+ 2, 12). Anal. Calcd for $C_{11}H_9ClN_2O_2$: C, 55.83; H, 3.83; N, 11.84; Cl, 14.98. Found: C, 55.75, H, 3.92; N, 11.67, Cl, 14.86.

4-[(2-Chlorophenyl)methylene]-2,4-dihydro-5-(hydroxymethyl)-3*H*-pyrazol-3-one (3d): mp 230–230.5 °C; ^1H NMR (Me_2SO-d_6) δ 5.03 (s, 3 H, 1 of 3 NaOD/D_2O exchangeable), 7.3–7.67 (m, 3 H), 7.83–8.16 (m, 1 H), 8.42 (s, 1 H), 11.83 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3450 and 3060 (OH, NH); 1720 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 236 (M^+, 30), 238 (M^+ 2, 10), 201 (100). Anal. Calcd for $C_{11}H_9ClN_2O_2$: C, 55.83; H, 3.83; N, 11.84. Found: C, 55.86; H, 3.80; N, 11.80.

4-(Phenylmethylene)-2,4-dihydro-5-(hydroxymethyl)-3*H*-pyrazol-3-one (3e): mp 201–202 °C; ^1H NMR (Me_2SO-d_6) δ 4.98 (s, 3 H, 1 of 3 NaOD/D_2O exchangeable), 7.32–7.88 (m, 5 H), 8.03 (s, 1 H), 11.23 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3450 and 3120 (OH, NH), 1720–1695 (br, C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 202 (M^+, 74). Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.86. Found: C, 65.48; H, 5.26; N, 14.11.

4-[(2-Nitrophenyl)methylene]-2,4-dihydro-5-(hydroxymethyl)-3*H*-pyrazol-3-one (3f): mp 213–214 °C; ^{1}NMR (Me_2SO-d_6) δ 4.95 (s, 3 H, 1 of 3 NaOD/D_2O exchangeable), 7.38–8.23 (m, 4 H, 8.35 (s, 1 H), 11.8 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3430 and 3130 (OH, NH), 1720 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 247 (M^+, 6), 135 (100), 136 (39). Anal. Calcd for $C_{11}H_9N_3O_4$: C, 53.44; H, 3.67, N, 17.00. Found: C, 53.21; H, 3.74; N, 16.90.

4-[(1,3-Benzodioxol-5-yl)methylene]-2,4-dihydro-5-(hydroxymethyl)-2-methyl-3*H*-pyrazol-3-one (3g): mp 228–229 °C; ^1H NMR (Me_2SO-d_6) δ 3.33 (s, 3 H), 5.07 and 5.13 (2 s, 3 H), 6.07 (s, 2 H), 6.82–7.38 (m, 3 H), 7.93 (s, 1 H); IR (KBr) 3340 (OH), 1725 (C=O) cm^{-1}; mass spectrum, m/e 260 (M^+). Anal. Calcd for $C_{13}H_{12}N_2O_4$: C, 59.99; H, 4.65; N, 10.77. Found: C, 60.00; H, 4.67; N, 10.82.

4-[(3,4-Dimethoxyphenyl)methylene]-2,4-dihydro-5-(hydroxymethyl)-2-methyl-3*H*-pyrazol-3-one (3h): mp 248–249 °C; ^1H NMR (Me_2SO-d_6) δ 3.67 (s, 3 H), 4.13 (s, 6 H), 5.5 (s, 3 H), 7.23–7.73 (m, 3 H), 8.1 (s, 1 H); IR (KBr) 3450 (OH), 1730 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 276 (M^+, 100). Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.84; H, 5.63; N, 10.36.

4-[(3,4,5-Trimethoxyphenyl)methylene]-2,4-dihydro-5-(hydroxymethyl)-2-methyl-3*H*-pyrazol-3-one (3i): mp 208–209 °C; ^1H NMR (Me_2SO-d_6) δ 3.4 (s, 3 H), 3.77 (s, 3 H), 3.83 (s, 6 H), 5.17 and 5.22 (2s, 3 H), 7.07 (s, 2 H), 7.93 (s, 1 H); IR (KBr) 3450 (OH), 1740 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 306 (M^+, 100). Anal. Calcd for $C_{15}H_{18}N_2O_5$: C, 58.81; H, 5.92; N, 9.15. Found: C, 59.00; H, 5.72; N, 9.10.

4-[(4-Chlorophenyl)methylene]-2,4-dihydro-5-(hydroxymethyl)-2-methyl-3*H*-pyrazol-3-one (3j): mp 221–222 °C; ^1H NMR (Me_2SO-d_6) δ 3.42 (s, 3 H), 5.15 and 5.25 (2 s, 3 H), 7.42–7.97 (A_2B_2 pattern, 4 H), 8.00 (s, 1 H); IR (KBr) 3450 (OH), 1720 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 250 (M^+, 59), 252 (M + 2, 21). Anal. Calcd for $C_{12}H_{11}ClN_2O_2$: C, 57.49; H, 4.42; N, 11.18. Found: C, 57.72; H, 4.06; N, 11.14.

4-(Phenylmethylene)-2,4-dihydro-5-(hydroxymethyl)-2-methyl-3*H*-pyrazol-3-one (3k): mp 232–232.5 °C (sharp); ^1H NMR (Me_2SO-d_6) δ 3.45 (s, 3 H), 5.21 and 5.30 (2 s, 3 H), 7.4–8.16 (m, 4 H), 8.2 (s, 1 H); IR (KBr) 3440 (OH), 1715 (C=O) cm^{-1}; mass spectrum, m/e 216 (M^+). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.67; H, 5.48; N, 12.94.

Preparation of 10-Aryl-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-ones 5. General Method. To the appropriate 3-(arylmethylene)-2,4(3*H*,5*H*)-furandione (**2**) (2 mmol) in absolute ethanol (2 mL) was added 2-aminothiophenol (*4*, 2 mmol) dissolved in absolute ethanol (1 mL) followed by concentrated hydrochloric acid (0.17 mL). The magnetically stirred solution was refluxed for 1 h under nitrogen. The reaction mixture was cooled, and the precipitated product was isolated by filtration and then washed with cold ethanol. In most cases the isolated material was very pure. Analytical samples were recrystallized from 2-propanol. The following compounds were prepared in this manner.

10-(1,3-Benzodioxol-5-yl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5a): mp 267–268 °C; ^1H NMR (Me_2SO-d_6) δ 5.02 (s, 2 H), 5.28 (s, 1 H), 5.93 (s, 2 H), 6.17–7.5 (m, 7 H), 10.27 (s, 1 H, NaOD/D_2O exchangeable); ^{13}C NMR (Me_2SO-d_6) 46.7, 66.8, 99.2, 100.8, 107.1, 107.8, 120.2, 120.9, 123.3, 129.1, 136.0, 144.6, 145.7, 146.9, 158.7, 172.1 ppm; IR (KBr) 3300 (NH), 1720 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 339 (M^+, 79), 281 (100), 280 (81). Anal. Calcd for $C_{18}H_{13}NO_4S$: C, 63.70; H, 3.86; N, 4.13. Found: C, 63.59; H, 4.10; N, 4.05.

10-(3,4-Dimethoxyphenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5b): mp 224–225 °C; ^1H NMR (Me_2SO-d_6) δ 3.55 (s, 3 H), 3.65 (s, 3 H), 5.02 (s, 2 H), 5.28 (s, 1 H), 6.38–7.55 (m, 7 H), 10.27 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3320 (NH), 1750 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 355 (M^+, 64), 296 (100). Anal. Calcd for $C_{19}H_{17}NO_4S$: C, 64.22; H, 4.82; N, 3.94. Found: C, 64.18; H, 4.88; N, 3.54.

10-(3,4,5-Trimethoxyphenyl)-4,10-dihydro-1*H*,3*H*-furo-[3,4-*c*][1,5]benzothiazepin-1-one (5c): mp 148–149 °C; ^1H NMR (Me_2SO-d_6) δ 3.53 (s, 9 H), 5.02 (s, 2 H), 5.27 (s, 1 H), 6.27 (s, 2 H), 6.87–7.5 (m, 4 H), 10.27 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1725 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 385 (M^+, 100). Anal. Calcd for $C_{20}H_{19}NO_5S$: C, 62.32; H, 4.97; N, 3.63. Found: C, 61.86; H, 5.09; N, 3.68.

10-(4-Chlorophenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*]-[1,5]benzothiazepin-1-one (5d): mp 286–287 °C; ^1H NMR (Me_2SO-d_6) δ 5.02 (s, 2 H), 5.37 (s, 1 H), 6.77–7.5 (m, 8 H), 10.33 (s, 1 H, NaOD/D_2O exchangeable); ^{13}C NMR (Me_2SO-d_6) δ 46.2, 66.9, 98.6, 121.0, 122.2, 123.3, 127.6, 128.8, 129.3, 136.0, 141.0, 144.6, 158.9, 172.0 ppm; (KBr) 3290 (NH), 1720 (C=O) cm^{-1}; mass spectrum, m/e (relative intensity) 329 (M_+, 65), 331 (M + 2, 27), 272 (100), 271 (75). Anal. Calcd for $C_{17}H_{12}ClNO_2S$: C, 61.91; H, 3.67; N, 4.25. Found: C, 61.80; H, 4.10; N, 4.03.

10-(2-Chlorophenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5e): mp 265–266 °C; ^{1}H NMR (Me_2SO-d_6) δ 5.03 (s, 2 H), 5.47 (s, 1 H), 6.33–7.73 (m, 8 H), 10.35 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1725 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 329 (M^+, 75), 331 (M + 2, 26), 236 (100). Anal. Calcd for $C_{17}H_{12}ClNO_2S$: C, 61.91; H, 3.67; N, 4.25. Found: C, 61.76; H, 3.77; N, 4.15.

10-(4-Bromophenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5f): mp 284–285 °C; ^{1}H NMR (Me_2SO-d_6) δ 5.02 (s, 2 H), 5.37 (s, 1 H), 6.7–7.57 (m, 8 H), 10.35 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1720 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 373 (M^+, 79), 375 (M + 2, 76). Anal. Calcd for $C_{17}H_{12}BrNO_2S$: C, 54.55; H, 3.23; N, 3.74. Found: C, 54.48; H, 3.56; N, 3.50.

10-Phenyl-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5g): mp 256–256.5 °C; ^{1}H NMR (Me_2SO-d_6) δ 4.97 (s, 2 H), 5.27 (s, 1 H), 6.70–7.5 (m, 9 H), 10.17 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1730 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 295 (M^+, 81), 236 (100). Anal. Calcd for $C_{17}H_{13}NO_2S$: C, 69.14; H, 4.44; N, 4.74. Found: C, 69.15; H, 4.61; N, 4.66.

10-(2-Nitrophenyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5h): mp 252–253 °C; ^{1}H NMR (Me_2SO-d_6) δ 5.1 (s, 2 H), 6.03 (s, 1 H), 6.67–7.63 (m, 6 H), 7.87–8.17 (m, 1 H), 10.38 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1725 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 340 (M^+, 2.4), 148 (100), 135 (99). Anal. Calcd for $C_{17}H_{12}N_2O_4S$: C, 59.99; H, 3.56; N, 8.23. Found: C, 59.52; H, 3.86; N, 8.28.

10-(5-Methyl-2-thienyl)-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-one (5i): mp 235–236 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.22 (s, 3 H), 4.92 (s, 2 H), 5.37 (s, 1 H), 6.3 (s, 2 H), 6.71–7.52 (m, 4 H), 10.17 (s, 1 H, NaOD/D_2O exchangeable); IR (KBr) 3300 (NH), 1720 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 315 (M^+, 100). Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 60.93; H, 4.15; N, 4.44. Found: C, 61.04; H, 4.18; N, 4.34.

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Registry No. **2** (Ar = 3,4-(methylenedioxy)phenyl), 87191-93-3; **2** (Ar = 3,4,5-trimethoxyphenyl), 87191-94-4; **2** (Ar = 4-chlorophenyl), 87191-95-5; **2** (Ar = 2-chlorophenyl), 87191-96-6; **2** (Ar = phenyl), 30030-96-7; **2** (Ar = 2-nitrophenyl), 87191-97-7; **2** (Ar = 3,4-dimethoxyphenyl), 87191-98-8; **2** (Ar = 4-bromophenyl), 87192-09-4; **2** (Ar = 5-methyl-2-thienyl), 87192-10-7; **3a**, 87191-99-9; **3b**, 87192-00-5; **3c**, 87192-01-6; **3d**, 87192-02-7; **3e**, 87192-03-8; **3f**, 87192-04-9; **3g**, 87192-05-0; **3h**, 87192-06-1; **3i**, 87207-11-2; **3j**, 87192-07-2; **3k**, 87192-08-3; **5a**, 87192-11-8; **5b**, 87192-12-9; **5c**, 87192-13-0; **5d**, 87192-14-1; **5e**, 87192-15-2; **5f**, 87192-16-3; **5g**, 87192-17-4; **5h**, 87192-18-5; **5i**, 87192-19-6.

Intramolecular Diels–Alder Reactions of Alkenylallenes. A Model Study for the Bottom Half of Chlorothricolide

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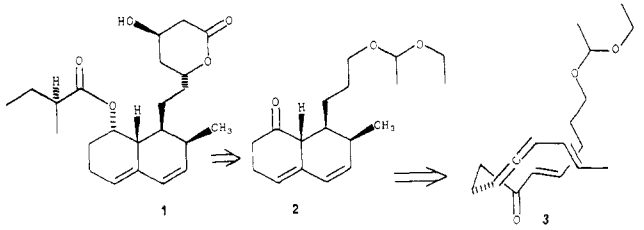
The intramolecular Diels–Alder reactions of two methyl (*E,E*)-2,7,8,10-dodecatetraenoates (**8a** and **9a**) and methyl (*E,E*)-2,6,7,9-undecatetraenoate (**8b**) have been examined. Alkenylallenes **8a** and **9a** react at 110–130 °C to give **10a** and **11a** stereospecifically. Alkenylallene **8b** undergoes an intramolecular Diels–Alder reaction to give **10b** at or below room temperature. Adduct **11a** is converted to **17**, a model for the bottom half of chlorothricolide, by epoxidation, rearrangement (BF_3), and reduction.

Our plan for the synthesis of the hypocholesterolemic agent compactin (**1**)[2] led us to consider an intramolecular Diels–Alder reaction of **3**, in which an alkenylallene is the



diene component, to give **2**, which contains three of the four chiral centers and the diene unit of the hexahydronaphthalene moiety of **1**. Although the use of alkenylallenes as dienes in Diels–Alder reactions is well-known,[3] intramolecular Diels–Alder reactions of alkenylallenes were virtually unexplored.[4]

The successful synthesis of **3** and its conversion to **2**[5] prompted the study of the scope of the intramolecular Diels–Alder reaction of alkenylallenes reported here. Several features of this reaction make it a particularly attractive synthetic method. The required alkenylallenes can be easily synthesized by methods not applicable to normal dienes. The allene moiety is chiral and can be

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