Synthesis and Reactions of Halo-, Nitro-, and Arylazo-substituted 3-Cinnamoyltropolones. Formation of Styryl-substituted Heterocycle-fused Troponoid Compounds

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3-Cinnamoyltropolone (**1**) reacted with bromine to afford 7-bromo- (**2**), 5,7-dibromo-3-cinnamoyltropolone (**3**), and 6,8-dibromo-4,9-dihydrocyclohepta[*b*]pyrane-4,9-dione (**4**) according to amount of the reagent. Iodination and nitration of **1** gave respectively 7-iodo- (**5**) and 5-nitro-3-cinnamoyltropolone (**6**). Azo-coupling reactions gave 5-arylazo-3-cinnamoyltropolones **7a-f**. Compounds **1**, **2**, **3** and **5** reacted with hydroxylamine to give 3-styryl-8*H*-cyclohept[*d*]isoxazol-8-ones **10-13**, while **6** and **7a** gave 5-nitro-3-styryl-8*H*-cyclohept[*d*]-isoxazol-8-one oxime (**14**) and 2-cinnamoyl-7-methoxy-4-phenylazotropone (**15**), respectively. The reactions of **1**, **3**, and **5** with phenylhydrazine gave 3-styryl-1,8-dihydrocycloheptapyrazol-8-ones **16-19**.

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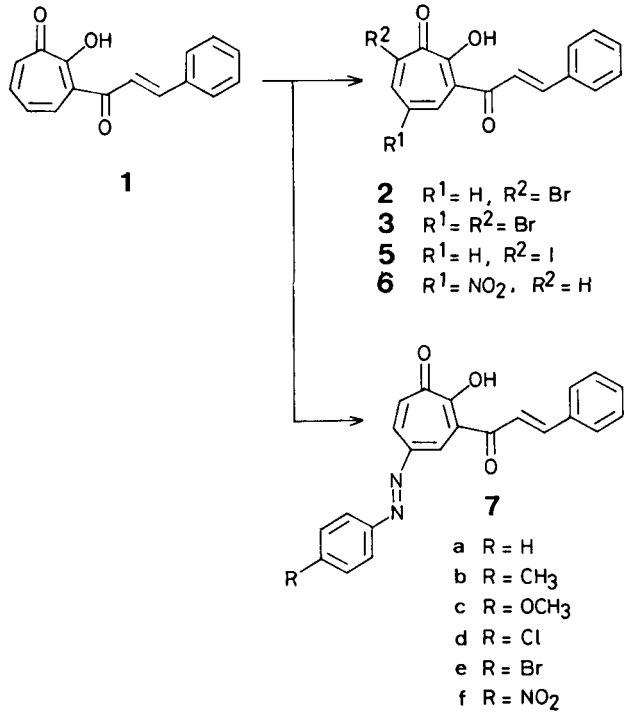
The tropolone nucleus is well known to susceptible to many electrophilic substitution reactions [1-4]. We also investigated the electrophilic reactions of 3-acetyl- [5] and 3-acetamidotropolone [6]. Recently, we reported that 3-cinnamoyltropolones were prepared by the condensation of 3-acetyltropolone with benzaldehydes [7]. These have similar structure to 2'-hydroxychalcones and have three reactive parts for electrophilic reagents. Two of them are seven-membered tropolone ring and six-membered benzene ring. The rest is propenoyl part between the two rings. Therefore, the reactions of 3-cinnamoyltropolones with electrophilic reagents are interesting. On the other hand, the reactions with nucleophilic reagents are also of interest for participation of tropolone ring, since chalcones reacted with hydroxylamine [8,9] and hydrazines [10,11] at the propenoyl moiety to give respectively diaryl-substituted isoxazolines and pyrazolines.

This paper deals with preparation of bromo-, iodo-, nitro-, and arylazo-substituted 3-cinnamoyltropolones by the electrophilic reactions and the conversion of the products to styryl-substituted isoxazole- and pyrazole-fused tropones.

Results and Discussion.

When 3-cinnamoyltropolone (**1**) was treated with an equimolar amount of bromine in acetic acid in the presence of sodium acetate to afford 7-bromo-3-cinnamoyltropolone (**2**) in 71% yield. The bromination with two and three equivalents of bromine gave respectively 5,7-dibromo-3-cinnamoyltropolone (**3**) in 75% yield and 6,8-dibromo-2-phenyl-4,9-dihydrocyclohepta[*b*]pyrane-4,9-dione (**4**) in 34% yield. The structure of **2** and **3** were confirmed from elemental analyses and the similarity of the spectra to those of bromo-substituted 3-acetyl- [5] and 3-acetamidotropolone [6]. The structure of **4** was determined on the basis of negative coloring test with iron(III) chloride and spectral data as well as on elemental analysis ($C_{16}H_8Br_2O_3$). In the ir spectrum, an absorption for the hydroxyl group is not observed and the two typical carbonyl absorptions for the tropone and pyrone moiety are observed at 1705 and 1648 cm^{-1}, respectively. The ^1H nmr spectrum shows two doublet peaks at δ 7.75 (d, 1H, J = 1.9 Hz) for H-7 and 8.73 (d, 1H, J = 1.9 Hz) for H-5, besides multiplet peak at δ 7.3-8.1 for Ph and H-3 protons. In this reaction, two

Scheme 1

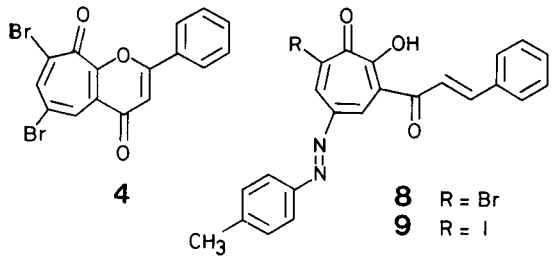


molar equivalents of bromine gave the dibromo compound **3** *via* monobromo compound **2** and the third bromine molecule added to the exocyclic carbon-carbon double bond to form dibromide which cyclized to give the product **4**. This mechanism might be supported by similar cyclization reaction in the 2'-hydroxychalcones gave flavones *via* 2'-hydroxychalcone dibromide [12]. On the other hand, the iodination of tropolone requires the presence of carbonate. The reaction of 3-cinnamoyltropolone (**1**) with iodine in the presence of potassium carbonate afforded 3-cinnamoyl-7-iodotropolone (**5**). Its structure was confirmed from elemental analysis ($C_{16}H_{11}IO_3$) and spectral data.

Although the nitration of 3-acetyltropolone gave 5-nitro- and 5,7-dinitro-sustituted product [5], 3-cinnamoyltropolone (**1**) treated with concentrated and fuming nitric acid to give 3-cinnamoyl-5-nitrotropolone (**6**) as the sole product. It was determined from its elemental analysis ($C_{16}H_{11}NO_5$) and spectral data. The ir spectrum shows three typical absorptions at 3120 (OH), 1670 (cinnamoyl C=O), and 1628 cm^{-1} (tropone C=O). In the ^1H nmr spectrum, three peaks for the neighboring protons in the tropone nucleus are observed at δ 7.50 (d, 1H, J = 11.2 Hz) for H-7, 8.10 (dd, 1H, J = 11.2, 2.1 Hz) for H-6, and 8.70 (d, 1H, J = 2.1 Hz) for H-4, besides multiplet peaks at δ 7.25-8.0 for phenyl and olefinic protons. In addition, the nitrosation of 3-cinnamoyltropolone (**1**) gave black tarry material and any product was not isolated.

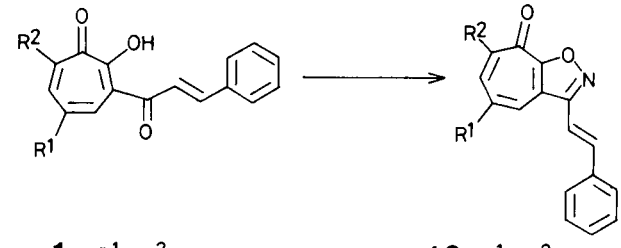
The azo-coupling reaction of tropolone takes place exclusively at the 5-position to give crystalline dyes. The reactions of 3-cinnamoyltropolone (**1**) with arenediazonium salts gave 5-arylazo-substituted 3-cinnamoyltropolones **7a-f** in good yields. The structures were confirmed from elemental analyses and spectral data (see Experimental). The 7-bromo- (**2**) and 7-iodo-3-cinnamoyltropolone (**5**) were also reacted with *p*-toluenediazonium salt to afford 7-bromo- (**8**) and 7-iodo-3-cinnamoyl-5-(4-methylphenylazo)tropolone (**9**) in 41 and 75% yields, respectively. Furthermore, the bromination of 3-cinnamoyl-5-phenylazotropolone (**7a**) gave 5,7-dibromo-3-cinnamoyltropolone (**3**). The ipso-substitution at the 5-position was observed, besides normal substitution at the 7-position.

Figure 1



As attacking site of nucleophilic reagents, chalcones have an enone moiety which connects two benzene ring. Thus, it has been reported that the chalcones react with hydroxylamine [8,9] and hydrazine [10,11] to afford respectively diphenyl-substituted isoxazolines and pyrazolines. On the other hand, we found that 3-acetyltropolone reacted with various nucleophilic reagents bearing two reactive sites to give a wide variety of heterocycle-fused troponoid compounds [13]. For examples, the reactions with hydroxylamine [14] and hydrazines (hydrazine [15], methylhydrazine [16], and phenylhydrazine [17]) gave respectively 8*H*-cyclohept[*d*]isoxazol-8-ones and 1,8-dihydrocycloheptapyrazol-8-ones.

Scheme 2

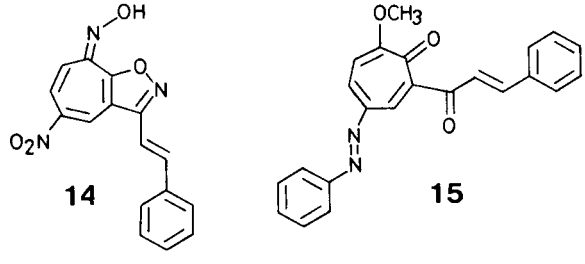


1 $R^1 = R^2 = H$
2 $R^1 = H$, $R^2 = Br$
3 $R^1 = R^2 = Br$
5 $R^1 = H$, $R^2 = I$

10 $R^1 = R^2 = H$
11 $R^1 = H$, $R^2 = Br$
12 $R^1 = R^2 = Br$
13 $R^1 = R$, $R^2 = I$

The reactions of 3-cinnamoyltropolone (**1**) with hydroxylamine in refluxing ethanol gave 3-styryl-8*H*-cyclohept[*d*]-isoxazol-8-one (**10**) in 59% yield. Its ^1H nmr spectrum shows an unresolved complex peaks at δ 7.1-8.1. In the ir spectrum, the characteristic hydroxyl and carbonyl absorptions for tropolone and the carbonyl group in the side chain disappeared, the tropone carbonyl absorption appeared at 1630 cm^{-1}. The elemental analysis ($C_{16}H_{11}NO_2$) supported the structure. The 7-bromo-, 5,7-dibromo-, and 7-iodo-substituted 3-cinnamoyltropolones **2**, **3** and **5** also afforded the corresponding halo-substituted 3-styryl-8*H*-cyclohept[*d*]isoxazol-8-ones **11**, **12** and **13**. These structures were determined on the basis of the spectral data as well as on elemental analyses. However, 3-cinnamoyl-5-nitrotropolone (**6**) reacted with hydroxylamine under the

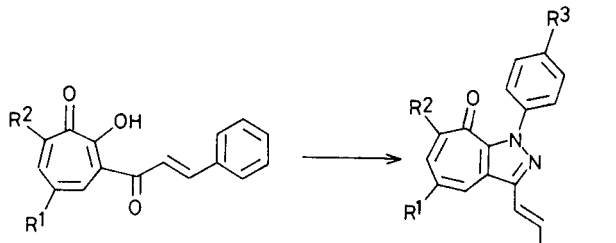
Figure 2



same conditions to afford 5-nitro-3-styryl-8*H*-cyclohept[*d*]-isoxazol-8-one oxime (**14**) in 26% yield. Its structure was determined from elemental analysis ($C_{16}H_{11}N_3O_4$) and spectral data. The ^1H nmr spectrum shows peaks at δ

7.2-7.8 (m, 7H) for CH=CH-Ph, 7.29 (d, 1H, J = 7.7 Hz) for H-7, 7.79 (dd, 1H, J = 7.7, 1.1 Hz) for H-6, 8.30 (d, 1H, J = 1.1 Hz) for H-4, and 12.47 (br s, 1H) for =N-OH group. The formation of compound **14** might depend on enhancement of the reactivity of tropone nucleus for nucleophilic reactions by strong electron-withdrawing effect of the nitro group. Furthermore, in the reactions of 3-cinnamoyl-5-phenylazotropolone (**7a**) with hydroxylamine gave the unusual product, 2-cinnamoyl-7-methoxy-5-phenylazotropone (**15**) in 24% yield. The structure was confirmed from elemental analysis ($C_{23}H_{18}N_2O_3$) and spectral data. The ir spectrum shows two absorptions for carbonyl group in the side-chain and tropone were observed at 1701 and 1652 cm^{-1}, respectively. In the ^1H nmr spectrum, a singlet peak for methoxyl protons were observed at δ 3.78, three peaks for the protons in the tropone ring being observed at δ 7.69 (d, 1H, J = 9.2 Hz) for H-6, 7.95 (dd, 1H, J = 9.2, 1.1 Hz) for H-5, and 8.11 (d, 1H, J = 1.1 Hz) for H-3. Thus, this compound **15** might be produced by etherification with methanol which was used as solvent.

Scheme 3



1 $R^1=R^2=H$
3 $R^1=R^2=Br$
5 $R^1=H$, $R^2=I$

16 $R^1=R^2=R^3=H$
17 $R^1=R^2=H$, $R^3=NO_2$
18 $R^1=R^2=Br$, $R^3=H$
19 $R^1=R^3=H$, $R^2=I$

When a solution of 3-cinnamoyltropolone (**1**) and phenylhydrazine in methanol was refluxed for 24 hours, the cyclized product, 1-phenyl-3-styryl-1,8-dihydrocyclohept[*d*]isoxazol-8-one (**16**) was isolated in 37% yield. Its structure was confirmed from elemental analysis ($C_{22}H_{16}N_2O$) and spectral data. The ir spectrum shows the absorption for tropone carbonyl group at 1634 cm^{-1}. All the ring protons were observed as complex multiplet peaks at δ 7.7-8.25. The compound **1** reacted with 4-nitrophenylhydrazine to afford 1-(4-nitrophenyl)-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**17**) in 33% yield. The 5,7-dibromo-(**3**) and 7-iodo-3-cinnamoyltropolone (**5**) also reacted with phenylhydrazine to give the corresponding 1,8-dihydrocycloheptapyrazol-8-one derivatives **18** and **19**. These results are different from those of chalcones and suggests that the tropolone ring is more reactive for nucleophilic reagents than propenoyl part.

EXPERIMENTAL

Measurements.

The ir spectra were taken on a Perkin-Elmer 1730 spectrophotometer. The ^1H nmr spectra were recorded with a JEOL JNM-PMX60 spectrometer.

7-Bromo-3-cinnamoyltropolone (**2**).

To a stirred solution of 3-cinnamoyltropolone (**1**) (1.0 g, 4.0 mmoles) and sodium acetate (500 mg) in acetic acid (180 ml) was added dropwise a solution of bromine (640 mg, 4 mmoles) in acetic acid (5 ml) at room temperature. After additional stirring for 2 hours, the solvent was evaporated *in vacuo* to give greenish yellow solid, which was washed with water and recrystallized from ethyl acetate to afford 7-bromo-3-cinnamoyltropolone (**2**) as pale greenish yellow needles, yield 930 mg (71%), mp 159-160°; ir (potassium bromide): ν max 3120 (OH), 1670 (C=O), 1610 (C=O), 978 cm^{-1} (CH); ^1H nmr (deuteriochloroform): δ 7.00 (dd, 1H, J = 10.0, 10.0 Hz, H-5), 7.25-7.8 (m, 7H), 7.71 (d, 1H, J = 10.0 Hz, H-6), 8.19 (d, 1H, J = 10.0 Hz, H-4).

Anal. Calcd. for $C_{16}H_{11}BrO_3$: C, 58.03; H, 3.55. Found: C, 57.92; H, 3.61.

3-Cinnamoyl-5,7-dibromotropolone (**3**).

A solution of bromine (1.28 g, 8.0 mmoles) in acetic acid (5 ml) was added dropwise to a stirred solution of 3-cinnamoyltropolone (**1**) (1.0 g, 4.0 mmoles) at room temperature to precipitate white solid after 10 minutes. The stirring was continued for an additional 1 hour. The precipitate was collected and recrystallized from ethyl acetate to give 3-cinnamoyl-5,7-dibromotropolone (**3**) as colorless needles, yield 1.22 g (75%), mp 198.5-199.5°; ir (potassium bromide): δ max 3050 (OH), 1660 (C=O), 1612 (C=O), 975 cm^{-1} (CH); ^1H nmr (deuteriochloroform): δ 7.2-7.6 (m, 7H), 7.90 (d, 1H, J = 2.0 Hz, H-6), 8.40 (d, 1H, J = 2.0 H).

Anal. Calcd. for $C_{16}H_{10}Br_2O_3$: C, 46.86; H, 2.46. Found: C, 46.72; H, 2.35.

6,8-Dibromo-2-phenyl-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (**4**).

A solution of bromine (480 mg, 3.0 mmoles) in acetic acid (2 ml) was added dropwise to a solution of 3-cinnamoyltropolone (**1**) (252 mg, 1.0 mmole) and sodium acetate (300 mg) in acetic acid (6 ml) to precipitate yellow crystals. After additional stirring for 2 hours, the reaction mixture was diluted with water. The precipitate was collected and recrystallized from ethyl acetate to give 6,8-dibromo-2-phenyl-4,9-dihydrocyclohepta-[*b*]pyran-4,9-dione (**4**) as yellow needles, yield 140 mg (34%), mp 258-259°; ir (potassium bromide): ν max 1705 (C=O), 1648 (C=O); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.3-8.1 (m, 7H), 7.75 (d, 1H, J = 1.9 Hz, H-7), 8.73 (d, 1H, J = 1.9 Hz, H-5).

Anal. Calcd. for $C_{16}H_8Br_2O_3$: C, 47.09; H, 1.98. Found: C, 46.93; H, 1.93.

3-Cinnamoyl-7-iodotropolone (**5**).

To a stirred mixture of 3-cinnamoyltropolone (**1**) (505 mg, 2.0 mmoles) and potassium carbonate (610 mg) in water (1.7 ml) was added a solution of iodine (650 mg) and potassium iodide (650 mg) in water (3.7 ml) in an ice-water bath. After stirring for 2 hours, an excess of iodine was reduced with sodium hydrogensulfite. The mixture was acidified with 6*M* hydrochloric acid to precipitate yellow crystals. The crystals were collected and recrystallized from methanol to give 3-cinnamoyl-7-iodotropolone (**5**) as yellow prisms, yield 352 mg (47%), mp 156-157°; ir (potassium bromide): ν max 3200 (OH), 1680 (C=O), 1620 cm^{-1} (C=O); ^1H nmr (deuteriodimethyl sulfoxide): δ 6.63 (dd, 1H, J = 9.9, 9.8 Hz, H-5), 6.9-7.3 (m, 7H), 7.67 (d, 1H, J = 9.9 Hz, H-6), 8.43 (d, 1H, J = 9.8 Hz, H-4).

Anal. Calcd. for $C_{16}H_{11}IO_3$: C, 50.82; H, 2.93. Found: C, 50.75; H, 2.87.

3-Cinnamoyl-5-nitrotropolone (**6**).

a) To an ice-cooled stirred solution of 3-cinnamoyltropolone (**1**) (505 mg, 2.0 mmoles) in acetic acid (4 ml) was added dropwise a mixture of fuming nitric acid (640 mg) and acetic acid (4 ml). The color of the mix-

ture changed from pale yellow to orange-red. After stirring for 2 hours, the precipitate was collected and recrystallized from chloroform to give 3-cinnamoyl-5-nitrotropolone (**6**) as yellow plates, yield 170 mg (29%), mp 206-207° dec; ir (potassium bromide): ν max 3120 (OH), 1670 (C=O), 1628 cm^{-1} (C=O); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.25-8.0 (m, 7H), 7.50 (d, 1H, J = 11.2 Hz, H-7), 8.10 (dd, 1H, J = 11.2, 2.1 Hz, H-6), 8.70 (d, 1H, J = 2.1 Hz, H-4).

Anal. Calcd. for $C_{16}H_{11}NO_5$: C, 64.64; H, 3.74; N, 4.71. Found: C, 64.71; H, 3.71; N, 4.54.

b) A concentrated (68%) nitric acid (400 mg) in acetic acid (2 ml) was added dropwise to an ice-cooled solution of 3-cinnamoyltropolone (**1**) (250 mg, 1.0 mmole) in acetic acid (2 ml). The mixture was stirred for 5 hours and worked up, as mentioned above, to give 3-cinnamoyl-5-nitrotropolone (**6**), yield 50 mg (17%).

Azo-coupling Reactions of 3-Cinnamoyltropolone (**1**).

To an ice-cooled stirred solution of 3-cinnamoyltropolone (**1**) (505 mg, 2.0 mmoles) in pyridines (6 ml) was added dropwise arenediazonium chloride solution, prepared from anilines (2.0 mmoles). After additional stirring for 2 hours, the precipitate was collected and recrystallized from benzene to give 3-cinnamoyl-5-arylazotropolone **7a-f**.

3-Cinnamoyl-5-phenylazotropolone (**7a**).

This compound was obtained in a yield of 625 mg (87%) as orange needles, mp 191-192° (dec); ir (potassium bromide): ν max 3350 (OH), 1680 (C=O), 1630 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 7.25-7.9 (m, 12H), 7.50 (d, 1H, J = 10.2 Hz, H-7), 8.35 (dd, 1H, J = 10.2, 2.4 Hz, H-6), 8.50 (d, 1H, J = 2.4 Hz, H-4).

Anal. Calcd. for $C_{22}H_{16}N_2O_3$: C, 74.14; H, 4.53; N, 7.86. Found: C, 74.38; H, 4.63; N, 7.85.

3-Cinnamoyl-5-(4-methylphenylazo)tropolone (**7b**).

This compound was obtained in a yield of 595 mg (80%) as orange needles, mp 176-177° dec; ir (potassium bromide): ν max 3250 (OH), 1670 (C=O), 1629 cm^{-1} (C=O).

Anal. Calcd. for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56. Found: C, 74.71; H, 4.82; N, 7.49.

3-Cinnamoyl-5-(4-methoxyphenylazo)tropolone (**7c**).

This compound was obtained in a yield of 580 mg (75%) as orange needles, mp 184° dec; ir (potassium bromide): ν max 3200 (OH), 1680 (C=O), 1620 cm^{-1} (C=O).

Anal. Calcd. for $C_{23}H_{18}N_2O_4$: C, 71.49; H, 4.70; N, 7.25. Found: C, 71.56; H, 4.75; N, 7.35.

5-(4-Chlorophenylazo)-3-cinnamoyltropolone (**7d**).

This compound was obtained in a yield of 626 mg (80%) as orange needles, mp 212° dec; ir (potassium bromide): ν max 3250 (OH), 1682 (C=O), 1628 cm^{-1} (C=O).

Anal. Calcd. for $C_{22}H_{15}ClN_2O_3$: C, 67.61; H, 3.87; N, 7.17. Found: 67.84; H, 3.74; N, 7.19.

5-(4-Bromophenylazo)-3-cinnamoyltropolone (**7e**).

This compound was obtained in a yield of 665 mg (61%) as orange needles, mp 222-223° dec; ir (potassium bromide): ν max 3270 (OH), 1688 (C=O), 1630 cm^{-1} (C=O).

Anal. Calcd. for $C_{22}H_{15}BrN_2O_3$: C, 60.70; H, 3.47; N, 6.44. Found: C, 60.48; H, 3.47; N, 6.35.

3-Cinnamoyl-5-(nitrophenylazo)tropolone (**7f**).

This compound was obtained in a yield of 603 mg (75%) as orange red needles, mp 223-224° dec; ir (potassium bromide): ν max 3280 (OH), 1688 (C=O), 1628 cm^{-1} (C=O).

Anal. Calcd. for $C_{22}H_{15}N_3O_5$: C, 65.83; H, 3.77; N, 10.47. Found: C, 65.99; H, 3.96; N, 10.41.

7-Bromo-3-cinnamoyl-5-(4-methylphenylazo)tropolone (**8**).

This compound was obtained from 7-bromo-3-cinnamoyltropolone (**2**) (331 mg, 1.0 mmole) in a yield of 182 mg (41%) as reddish orange needles, mp 214-215° dec; ir (potassium bromide): ν max 3150 (OH), 1668 (C=O), 1610 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.43 (s, 3H, CH_3), 7.2-7.9 (m, 11H), 8.33 (d, 1H, J = 2.1 Hz, H-6), 8.98 (d, 1H, J = 2.1 Hz, H-4).

Anal. Calcd. for $C_{23}H_{17}BrN_2O_3$: C, 61.49; H, 3.81; N, 6.24. Found: C, 61.89; H, 4.15; N, 6.02.

3-Cinnamoyl-7-iodo-5-(4-methylphenylazo)tropolone (**9**).

This compound was obtained from 3-cinnamoyl-7-iodotropolone (**5**) (378 mg, 1.0 mmole) in a yield of 371 mg (75%) as reddish orange needles, mp 204-205°; ir (potassium bromide): ν max 3190 (OH), 1665 (C=O), 1610 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.48 (s, 3H, CH_3), 7.1-7.9 (m, 11H), 8.34 (d, 1H, J = 3.0 Hz, H-6), 9.27 (d, 1H, J = 3.0 Hz, H-4).

Anal. Calcd. for $C_{23}H_{17}IN_2O_3$: C, 55.66; H, 3.45; N, 5.65. Found: C, 55.70; H, 3.39; N, 5.78.

Reaction of 3-Cinnamoyl-5-phenylazotropolone (**7a**) with Bromine.

To a stirred solution of 3-cinnamoyl-5-phenylazotropolone (**7a**) (180 mg, 0.5 mmole) and sodium acetate (100 mg) in acetic acid (5 ml) was added a solution of bromine (160 mg, 1.0 mmoles) in acetic acid (5 ml). After stirring for 5 hours, the precipitate was collected and recrystallized from ethyl acetate to give 3-cinnamoyl-5,7-dibromotropolone (**3**), yield 70 mg (34%).

3-Styryl-8*H*-cyclohept[*d*]isoxazol-8-one (**10**).

A solution of 3-cinnamoyltropolone (**1**) (755 mg, 3.0 mmoles) and hydroxylamine hydrochloride (420 mg, 6.0 mmoles) in absolute ethanol (30 ml) was refluxed for 12 hours. The precipitate was collected and recrystallized from ethanol to afford 3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one (**10**) as colorless scales, yield 440 mg (59%), mp 234-235°; ir (potassium bromide): ν max 1630 (C=O), 1621 cm^{-1} (C=N); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.1-8.1 (m, 11H).

Anal. Calcd. for $C_{16}H_{11}NO_2$: C, 77.09; H, 4.45; N, 5.62. Found: C, 76.95; H, 4.27; N, 5.45.

7-Bromo-3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one (**11**).

A solution of 7-bromo-3-cinnamoyltropolone (**2**) (330 mg, 1.0 mmole) and hydroxylamine hydrochloride (140 mg, 2.0 mmoles) in absolute ethanol (30 ml) was reflulxed for 10 hours. The precipitate was collected and recrystallized from ethyl acetate to afford 7-bromo-3-cinnamoyl-8*H*-cyclohept[*d*]isoxazol-8-one (**11**) as yellow needles, yield 151 mg (46%), mp 238-239°; ir (potassium bromide): ν max 1628 (C=O), 1592 cm^{-1} (C=N); ^1H nmr (deuteriodimethyl sulfoxide): δ 6.75 (dd, 1H, J = 10.8, 10.0 Hz, H-5), 7.2-7.6 (m, 7H), 7.90 (d, 1H, J = 10.8 Hz, H-6), 8.31 (d, 1H, J = 10.0 Hz, H-4).

Anal. Calcd. for $C_{16}H_{10}BrNO_2$: C, 58.56; H, 3.07; N, 4.27. Found: C, 58.71; H, 3.04; N, 4.22.

5,7-Dibromo-3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one (**12**).

A solution of 5,7-dibromo-3-cinnamoyltropolone (**3**) (210 mg, 0.5 mmole) and hydroxylamine hydrochloride (70 mg, 1.0 mmole) in absolute ethanol (30 ml) was refluxed for 15 hours. The precipitate was collected and recrystallized from ethyl acetate to afford 5,7-dibromo-3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one (**12**) as yellow scales, yield 120 mg (59%), mp 234-235°; ir (potassium bromide): ν max 1635 (C=O), 1581 cm^{-1} (C=O); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.35-8.9 (m, 7H), 7.96 (d, 1H, J = 1.8 Hz, H-6), 8.68 (d, 1H, J = 1.8 Hz, H-4).

Anal. Calcd. for $C_{16}H_9Br_2NO_2$: C, 47.21; H, 2.23; N, 3.44. Found: C, 47.18; H, 2.44; N, 3.49.

7-Iodo-3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one (**13**).

A solution of 7-iodo-3-cinnamoyltropolone (**5**) (150 mg, 0.4 mmole) and hydroxylamine hydrochloride (60 mg, 0.8 mmole) in absolute ethanol (12 ml) was refluxed for 24 hours. The mixture was diluted with water (15 ml) to precipitate yellow solid, which was collected and recrystallized from ethyl acetate to afford 7-iodo-3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one (**13**)

as yellow scales, yield 30 mg (20%), mp 248°; ir (potassium bromide): ν max 1631 (C=O), 1620 cm^{-1} (C=N); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.00 (dd, 1H, J = 10.0, 9.6 Hz, H-5), 7.0-7.8 (m, 7H), 8.08 (d, 1H, J = 10.0 Hz, H-6), 8.90 (d, 1H, J = 9.6 Hz, H-4).

Anal. Calcd. for $C_{16}H_{10}INO_2$: C, 51.22; H, 2.69; N, 3.73. Found: C, 51.27; H, 2.61; N, 3.60.

5-Nitro-3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one Oxime (**14**).

A solution of 3-cinnamoyl-5-nitrotropolone (**6**) (200 mg, 0.67 mmole) and hydroxylamine hydrochloride (95 mg, 1.7 mmoles) in absolute ethanol (20 ml) was refluxed for 36 hours. The precipitate was collected and recrystallized from acetic acid to afford 5-nitro-3-styryl-8*H*-cyclohept[*d*]isoxazol-8-one oxime (**14**) as red needles, yield 55 mg (27%), mp 254° dec; ir (potassium bromide): ν max 3270 (OH), 1634 cm^{-1} (C=O); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.2-7.8 (m, 7H), 7.29 (d, 1H, J = 7.7 Hz, H-7), 7.79 (dd, 1H, J = 7.7, 1.1 Hz, H-6), 8.30 (d, 1H, J = 1.1 Hz, H-4), 12.47 (br s, 1H, OH).

Anal. Calcd. for $C_{16}H_{11}N_3O_4$: C, 62.13; H, 3.59; N, 13.59. Found: C, 61.95; H, 3.46; N, 14.02.

2-Cinnamoyl-7-methoxy-5-phenylazotropone (**15**).

A solution of 3-cinnamoyl-5-phenylazotropolone (**7a**) (200 mg) and hydroxylamine hydrochloride (100 mg) in methanol (20 ml) was refluxed for 48 hours. The precipitate was collected and recrystallized from acetic acid to afford 2-cinnamoyl-7-methoxy-5-phenylazotropone (**15**) as red needles, yield 50 mg (24%), mp 176°; ir (potassium bromide): ν max 1701 (C=O), 1652 cm^{-1} (C=O); ^1H nmr (deuteriodimethyl sulfoxide): δ 3.78 (s, 3H, OCH_3), 7.3-7.7 (m, 12H), 7.69 (d, 1H, J = 9.2 Hz, H-6), 7.95 (dd, 1H, J = 9.2, 1.1 Hz, H-5), 8.11 (d, 1H, J = 1.1 Hz, H-3).

Anal. Calcd. for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56. Found: C, 74.74; H, 4.94; N, 7.76.

1-Phenyl-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**16**).

A mixture of 3-cinnamoyltropolone (**1**) (250 mg, 1.0 mmole) and phenylhydrazine hydrochloride (290 mg, 2.0 mmoles) in methanol (10 ml) was refluxed for 24 hours. The precipitate was collected and recrystallized from ethyl acetate to afford 1-phenyl-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**16**) as pale yellow needles, yield 120 mg (37%), mp 202-203°; ir (potassium bromide): ν max 1634 (C=O), 1595 cm^{-1} (C=N); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.7-8.25 (m, 16H).

Anal. Calcd. for $C_{22}H_{16}N_2O$: C, 81.46; H, 4.97; N, 8.64. Found: C, 81.70; H, 4.92; N, 8.53.

1-(4-Nitrophenyl)-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**17**).

A mixture of 3-cinnamoyltropolone (**1**) (250 mg, 1.0 mmole) and *p*-nitrophenylhydrazine (290 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 12 hours. The precipitate was collected and recrystallized from 1-butanol to afford 1-(4-nitrophenyl)-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**17**) as yellow needles, yield 120 mg (33%), mp 264-265°; ir (potassium bromide): ν max 1642 (C=O), 1618 cm^{-1} (C=N); ^1H nmr (deuteriodimethyl sulfoxide): δ 6.8-8.5 (m, 15H).

Anal. Calcd. for $C_{22}H_{15}N_3O_3$: C, 71.53; H, 4.09; N, 11.38. Found: C, 71.33; H, 4.14; N, 11.62.

5,7-Dibromo-1-phenyl-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**18**).

A mixture of 3-cinnamoyl-5,7-dibromotropolone (**3**) (200 mg, 0.5 mmole) and phenylhydrazine hydrochloride (145 mg, 1.0 mmole) in absolute ethanol (20 ml) was refluxed for 24 hours. The precipitate was collected and recrystallized from 1-butanol to afford 5,7-dibromo-1-phenyl-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**18**) as yellow needles, yield 123 mg (51%), mp 261-262°; ir (potassium bromide): ν max 1624 (C=O), 1592 cm^{-1} (C=N); ^1H nmr (deuteriodimethyl sulfoxide): δ 7.2-8.1 (m, 12H), 8.02 (d, 1H, J = 1.8 Hz, H-6), 8.91 (d, 1H, J = 1.8 Hz, H-4).

Anal. Calcd. for $C_{22}H_{14}Br_2N_2O$: C, 54.80; H, 2.93; N, 5.81. Found: C, 54.72; H, 2.94; N, 5.80.

7-Iodo-1-phenyl-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**19**).

A mixture of 7-iodo-3-cinnamoyltropolone (**5**) (200 mg, 0.53 mmole) and phenylhydrazine hydrochloride (150 mg, 1.05 mmoles) in absolute ethanol (15 ml) was refluxed for 12 hours. The precipitate was collected and recrystallized from 1-butanol to afford 7-iodo-1-phenyl-3-styryl-1,8-dihydrocycloheptapyrazol-8-one (**19**) as yellow needles, yield 80 mg (34%), mp 266-267°; ir (potassium bromide): ν max 1617 (C=O), 1589 cm^{-1} (C=N); ^1H nmr (deuteriodimethyl sulfoxide): δ 6.7-7.8 (m, 12H), 6.88 (dd, 1H, J = 10.5, 9.7 Hz, H-5), 8.23 (d, 1H, J = 10.5 Hz, H-6), 8.70 (d, 1H, J = 9.7 Hz, H-4).

Anal. Calcd. for $C_{22}H_{15}IN_2O$: C, 58.79; H, 3.36; N, 6.24. Found: C, 58.58; H, 3.41; N, 6.27.

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