

## The Reaction of Cyclohepta-2,6-dienone with Amines

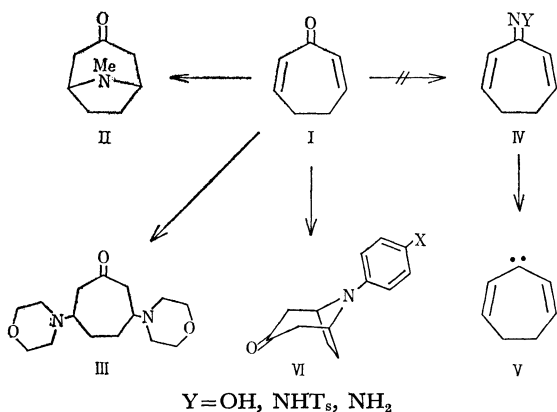
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Cyclohepta-2,6-dienone (I) was found to react with primary amines or secondary amines to afford tropinone-type adducts (II) or a 1:2 adduct such as III in good yields. We wish to describe the results here, including those of the reactions of I with some carbonyl reagents.

First of all, we attempted to synthesize oxime (IV: Y=OH), tosylhydrazone (IV: Y=NHTs), and hydrazone (IV: Y=NH<sub>2</sub>) in order to form cyclohepta-2,6-dienylidene (V) or its precursor, the diazo compound.<sup>1)</sup> However, the reaction of I with the corresponding carbonyl reagents resulted in the formation of resinous products, and we failed to isolate the expected product. An inspection of the IR and NMR spectra of the products indicates the absence of the C=C bond and an olefinic proton. This means an amino group of the reagents is added to the dienone system of I. For comparison with this behavior, the reactions of other amines with I were also investigated.



When cyclohepta-2,6-dienone (I) was treated with aqueous methylamine in an alcoholic solution, tropinone (II) could be obtained; this had been reported by Horák who, however, identified the formation of II by paper chromatography.<sup>2)</sup> Although this method was suggested by Robinson in 1917,<sup>3)</sup> it is a method of preparing tropinone in addition to variant methods discovered by Robinson,<sup>3)</sup> Willstätter,<sup>4)</sup> Schöpf,<sup>5)</sup> and Turro.<sup>6)</sup> The similar reaction of I with arylamines afforded *N*-arylnortropinone derivatives (VI) in fairly good yields, which are shown in Table I. The structure of the products could be elucidated on the basis of elemental analysis and a study of the IR, UV, and

NMR spectra (see Table I and Experimental section). Derivatives which possess an ethyl, isopropyl, benzyl or  $\beta$ -hydroxyethyl group at the *N*-position were synthesized by Robinson's method,<sup>7)</sup> whereas so far *N*-aryl derivatives have not been synthesized. Thus, the reaction of I with arylamines is a unique method for the synthesis of the *N*-arylnortropinones.

TABLE I. *N*-ARYL DERIVATIVES OF NORTROPINONE

| X in VI         | Mp (°C) | Yield (%) | IR(C=O) in KBr cm <sup>-1</sup> | UV in EtOH nm (log $\epsilon$ ) |
|-----------------|---------|-----------|---------------------------------|---------------------------------|
| OMe             | 134     | 93        | 1709                            | 250(4.14) 308(3.20)             |
| Me              | 96      | 68        | 1701                            | 252(4.14) 293(3.17)             |
| H               | 103     | 91        | 1704                            | 250(4.14) 287(3.22)             |
| Cl              | 155     | 73        | 1709                            | 258(4.16) 300(3.18)             |
| NO <sub>2</sub> | 202     | 45        | 1712                            | 231(3.58) 392(4.13)             |

When even 1 equivalent of morpholine was reacted with I at room temperature, a 2:1 adduct (III) was formed. As expected, the yield of III was increased by the use of 2 equivalents of the amine. The structure of III was proved by elemental analysis and by a study of the spectral data (see Experimental section).

The addition reaction of cross-conjugated  $\alpha,\beta$ -unsaturated ketones with amines has been known for a long time.<sup>8)</sup> Recently, it was found that, under irradiation, alcohols and acids added to I.<sup>9)</sup> In addition, the photochemical addition of diethylamine to cycloheptenone or cyclooctenone has also been reported.<sup>10)</sup> However, our experiment clarified that amines added readily to the enone system of I in the dark reaction, as had been reported before.<sup>8)</sup>

## Experimental

**Tropinone (II).** A 40% aqueous solution of methylamine (7 g, 90 mmol) was gradually added, under ice-cooling, to a solution of I (9.73 g, 90 mmol) dissolved in ethanol (15 ml). After the reaction mixture had been allowed to stand at a room temperature for 2 hr, it was extracted with ether. The evaporation of the ethereal extract, followed by the distillation of the residual oil, afforded an oil (bp 79—89°C/7 mmHg, 6.9 g, 55%) which partially crystallized on standing. The recrystallization of the crystalline part from cyclohexane provided needles, mp 41—42°C, which were identical with tropinone (lit, mp 42°C).<sup>3)</sup> It also afforded quaternary ammonium iodide, mp 266°C (lit, mp 265°C)<sup>11)</sup> in a quantitative yield when treated with methyl iodide in acetone.

***N*-Arylnortropinone (VI).** To a solution of I (432 mg,

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4 mmol) dissolved in ether (20 ml), we added aniline (372 mg, 4 mmol); the resulting mixture was allowed to stand at room temperature for 3 hr, during which period some crystals deposited. Filtration, followed by recrystallization from cyclohexane, provided needles (VI: X=H), mp 103°C (444 mg). The chromatography of a benzene-solution of a non-crystallized part on an alumina column afforded needles, mp 103°C (285 mg). The combined yield was 91%. The NMR spectrum in  $\text{CDCl}_3$  (60 MHz) showed  $\tau$  2.33–3.26 (5H, multiplet), 5.30 (2H, broad singlet), and 7.1–8.2 (8H, multiplet).

Other derivatives (VI: X=OMe, Me and Cl) could be obtained in a similar way, that is, by treating I with the corresponding base in an ethanolic solution. For the synthesis

TABLE 2. ELEMENTAL ANALYSES OF  
N-ARYLNORTROPINONES (VI)

|       | X=    | OMe   | Me    | H     | Cl    | $\text{NO}_2$ |
|-------|-------|-------|-------|-------|-------|---------------|
| C (%) | Found | 72.69 | 78.05 | 77.78 | 66.52 | 63.31         |
|       | Calcd | 72.70 | 78.10 | 77.58 | 66.24 | 63.40         |
| H (%) | Found | 7.51  | 8.25  | 7.81  | 6.14  | 5.95          |
|       | Calcd | 7.41  | 7.96  | 7.51  | 5.99  | 5.73          |
| N (%) | Found | 6.16  | 6.24  | 7.39  | 5.99  | 11.39         |
|       | Calcd | 6.06  | 6.51  | 6.96  | 5.94  | 11.38         |

of the *p*-nitrophenyl derivative (VI: X= $\text{NO}_2$ ), however, it was necessary to reflux the ethanolic solution containing I and *p*-nitroaniline (each 4 mmol in 10 ml) for 15 hr. The results of elemental analyses of the products are shown in Table 2.

*3,6-Dimorpholinocycloheptanone (III)*. Morpholine (1.74 g, 20 mmol) was gradually added under ice-cooling, to a solution of I (1.08 g, 10 mmol) dissolved in ethanol (5 ml). After standing for 12 hr at room temperature, the reaction mixture, then containing crystals deposited, was filtered to give pale yellow crystals, mp 109–117°C (956 mg). The concentration of the filtrate afforded other crystals, mp 122–123°C (890 mg) as a second crop. The chromatography of the non-crystallized portions on an alumina column provided crystals, mp 120°C (504 mg) (from petroleum-ether benzene fractions). Recrystallization from ethanol afforded III as colorless prisms, mp 124°C (2.08 g, 74%). IR in KBr for C=O, 1695  $\text{cm}^{-1}$ ; NMR spectrum in  $\text{CDCl}_3$  (60 MHz);  $\tau$  6.36 (8H, quartet), 7.33 (6H, broad singlet), 7.53 (8H, quartet), and 7.8–8.3 (4H, multiplet).

Found: C, 63.60; H, 9.27; N, 9.87%. Calcd for  $\text{C}_{15}\text{H}_{26}\text{O}_3\text{N}_2$ : C, 63.80; H, 9.28; N, 9.92%.

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