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Studies on Heterocyclic Analogs of Azulenes. III.[1] The Reactions of 2-Chloro-3-ethoxycarbonylcyclohepta[*b*]pyrrole with the Carbanions Derived from Active Methylene Compounds

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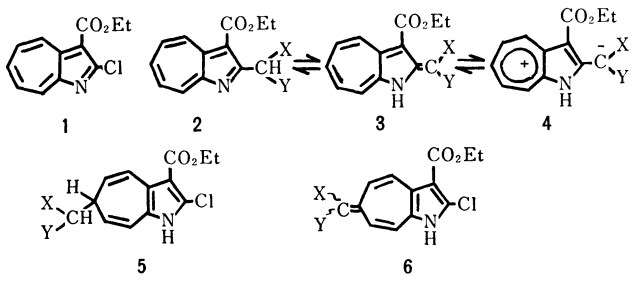
Synopsis. 2-Chloro-3-ethoxycarbonylcyclohepta[*b*]-pyrrole reacts with the carbanions derived from active methylene compounds to give substitution products and/or addition products depending on the reaction conditions.

2-Chloro-3-ethoxycarbonylcyclohepta[*b*]pyrrole (**1**) was reported by Matsumura to be substituted at C-2 with malononitrile in hot dioxane.[2] As our findings that **1** affords an addition product at C-8 when treated with Grignard reagents[3] led us to suspect the claim of Matsumura, we repeated his reaction. In our hands the reaction was more complicated than reported,[2] giving a number of products depending on the reaction conditions.

Treatment of **1** with malononitrile in boiling dioxane in the presence of sodium hydride produced two compounds in the ratio of 19: 1. The major one was the Matsumura's compound (**3a**), which is present as the methide form as confirmed by spectral methods, and the minor one was 1,6-dihydro-2-chloro-6-(dicyanomethylene)-3-(ethoxycarbonyl)cyclohepta[*b*]pyrrole(**6a**), a product formed by addition at C-6 of **1** followed by dehydrogenation. Reaction of **1** with ethyl cyanoacetate under the similar conditions afforded the corresponding **3b** and **6b** is the ratio of 4: 1. Although the reaction of **1** with phenylacetonitrile proceeded to give a substitution product and the compound (**6c**) in the ratio of 35: 1, the former takes the structure of 3-ethoxycarbonyl-2-(α-cyanobenzyl)cyclohepta[*b*]pyrrole (**2c**) in solid and in solution as shown by IR and NMR spectra. Predominant shift of the tautomeric equilibrium in favor of the 2-methylene forms (**3a**) and (**3b**), though unusual,[4] must be due to the high stability of the formal negative charge in **4**.

However, the product ratio changed dramatically when the reaction of **1** with ethyl cyanoacetate or phenylacetonitrile was undertaken at room temperature. For instance, the reaction with phenylacetonitrile yielded 1,6-dihydro-2-chloro-3-ethoxycarbonyl-6-(α-cyanobenzyl)cyclohepta[*b*]pyrrole (**5c**) (65%) and **6c** (2%) without giving a trace of **2c**. The structure of **5c** was proved by the presence of a 1H quartet at δ 2.63 and a 1H doublet at δ 4.05 in its NMR spectrum. **5** was unstable, changing into **6** on storage in air.



a: X=Y=CN; b: X=CN, Y=CO_2Et; c: X=CN, Y=Ph

Formation of the addition product **5** or its dehydrogenation product **6** was also observed when the reaction was carried out in ethanol in the presence of sodium ethoxide at room temperature or under reflux. These results are collected in Table 1. Dependence of the formations of the substitution product and the addition product[5] (or its dehydrogenation product) of **1** upon the solvent polarity and the reaction temperature is interesting, but we were unable to advance a rationale for these observations.

Table 1. Ratio of the substitution and addition products of **1**

Reagent	Conditions		Ratio (%)	
	Solvent	Temperature (°C)	Substitution (**2** or **3**)	Addition (**5**+**6**)
$CH_2(CN)_2$	Dioxane	25	70	30
$CH_2(CN)_2$	Dioxane	101	95	5
$CH_2(CN)_2$	EtOH	78	11	89
$CNCH_2CO_2Et$	Dioxane	25	21	79
$CNCH_2CO_2Et$	Dioxane	101	82	18
$CNCH_2CO_2Et$	EtOH	25	24	76
$PhCH_2CN$	Dioxane	25	0	100
$PhCH_2CN$	Dioxane	101	97	3
$PhCH_2CN$	EtOH	78	1	99

Experimental

Melting points were uncorrected. NMR spectra were recorded in $CDCl_3$ unless otherwise stated with a Varian HA-100 spectrometer at 100 MHz and the assignments were confirmed by decoupling techniques where necessary. IR spectra were obtained as Nujol mulls, and UV spectra were measured for chloroform solutions unless otherwise stated. Chromatography was performed on Kiesel gel 60 with chloroform. Yields are based on unrecovered starting materials.

*Reaction of **1** with Malononitrile.* (a) Malononitrile (2.00 g) was added into dry dioxane (100 ml) in which sodium hydride (66% in mineral oil) (0.70 g) was suspended. A solution of **1** (1.00 g) in dry dioxane (50 ml) was added into this mixture, stirred at room temperature for 2 days, acidified with acetic acid, and extracted with chloroform. The dried (Na_2SO_4) extracts were evaporated and the residue was chromatographed to give the starting material (0.771 g), **3a** (0.083 g, 30%), and **6a** (0.036 g, 17%), successively. **3a**: Red prisms

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(from chloroform), mp >300 °C (lit,[2] mp >260 °C), NMR (DMSO-d_6) δ=1.38 (3H, t, J=7 Hz), 4.38 (2H, q, J=7 Hz), 7.7—8.3 (4H, m), 8.67 (1H, bd, J=10 Hz);[6] UV_{max} (MeOH) 257 nm (log ε 4.26), 290 (4.32), 336 (3.78), 438 (4.29); IR 3140 (NH), 2200 (C≡N), 2150 (C≡N), 1680 cm^{-1} (C=O). Found: C, 67.75; H, 4.03; N, 15.69%. **6a**: Yellow needles (from chloroform), mp >300 °C, NMR (DMSO-d_6) δ=1.38 (3H, t, J=7 Hz), 4.33 (2H, q, J=7 Hz), 7.12 (1H, dd, J=12 and 2 Hz), 7.16 (1H, dd, J=12 and 2 Hz), 7.44 (1H, d, J=12 Hz), 8.22 (1H, d, J=12 Hz);[6] UV_{max} 260 nm (log ε 4.29), 282 (4.02), 290^{sh} (4.02), 433 (4.51), 448^{sh} (4.48), 472^{sh} (4.17); IR 3100 (NH), 2200 (C≡N), 1695 cm^{-1} (C=O). Found: C, 59.95; H, 3.18; Cl, 12.01; N, 14.03%. Calcd for $C_{15}H_{10}ClN_3O_2$: C, 60.13; H, 3.36; Cl, 11.84; N, 14.02%. (b) When the above reaction (**1** (2.00 g), dioxane (50 ml), NaH (1.40 g) in dioxane (100 ml), and the nitrile (4.00 g)) was repeated under reflux for 2 h, **3a** (2.074 g, 92%) and **6a** (0.106 g, 4%) were obtained. (c) The nitrile (2.00 g) was added into a solution of sodium ethoxide (Na (0.40 g) and abs ethanol (80 ml)). A solution of **1** (1.00 g) in abs ethanol (40 ml) was added into this mixture, heated under reflux for 1 h, and worked up as above to give **5a** (0.037 g, 4%), the starting material (0.306 g), **3a** (0.060 g, 7%), and **6a** (0.461 g, 52%), successively. **5a**: Needles (from cyclohexane), mp 118—120 °C, NMR δ=1.40 (3H, t, J=7 Hz), 2.46 (1H, q, J=7 Hz), 4.30 (1H, d, J=7 Hz), 4.35 (2H, q, J=7 Hz), 5.2—5.6 (2H, m), 6.40 (1H, d, J=9.5 Hz), 7.01 (1H, d, J=9.5 Hz), 8.92 (1H, bs); IR 3200 (NH), 2200 (C≡N), 1670 cm^{-1} (C=O). **5a** was unstable, changing into **6a** in 27% yield on storage for 5 days.

*Reaction of **1** with Ethyl Cyanoacetate.* (a) A solution of **1** (1.00 g) in dry dioxane (40 ml) was added into a mixture of ethyl cyanoacetate (1.00 g), sodium hydride (0.70 g), and dry dioxane (40 ml), stirred at room temperature for 1 day, and worked up as above to give **5b** (0.210 g, 16%), the starting material (0.133 g), **3b** (0.206 g, 18%), and **6b** (0.576 g, 52%), successively. **5b**: Needles (from cyclohexane), mp 130—132 °C, NMR δ=1.37 (3H, t, J=7 Hz), 1.39 (3H, t, J=7 Hz), 2.39 (1H, t, J=6.5 Hz), 3.05 (1H, d, J=6.5 Hz), 4.32 (2H, q, J=7 Hz), 4.34 (2H, q, J=7 Hz), 5.4—5.6 (2H, m), 6.39 (1H, d, J=10 Hz), 7.00 (1H, d, J=10 Hz), 8.85 (1H, bs); IR 3200 (NH), 2200 (C≡N), 1675 (C=O), 1663 cm^{-1} (C=O). **3b**: Red needles (from benzene), mp 163—165 °C (lit,[2] mp 163—165 °C), NMR δ=1.37 (3H, t, J=7 Hz), 1.46 (3H, t, J=7 Hz), 4.31 (2H, q, J=7 Hz), 4.51 (2H, q, J=7 Hz), 7.3—7.7 (4H, m), 8.53 (1H, bd, J=10.5 Hz); UV_{max} 259 nm (log ε 4.39), 292 (4.42), 341 (3.98), 500 (4.18). **6b**: Orange plates (from benzene), mp 255—256 °C (dec), NMR (DMSO-d_6) δ=1.27 (6H, t, J=7 Hz), 1.35 (6H, t, J=7 Hz), 4.15 (4H, q, J=7 Hz), 4.27 (4H, q, J=7 Hz), 7.14 (1H, dd, J=12 and 2 Hz), 7.21 (2H, d, J=12.5 Hz), 7.36 (1H, d, J=12 Hz), 7.94 (1H, d, J=12.5 Hz), 8.04 (1H, d, J=12.5 Hz), 8.48 (1H, dd, J=12.5 and 1.5 Hz), 8.56 (1H, d, J=12.5 and 2 Hz);[6,7] UV_{max} 258 nm (log ε 4.42), 281 (4.17), 444 (4.56); IR 3150 (NH), 2200 (C≡N), 1695 (C=O), 1650 cm^{-1} (C=O). Found: C, 58.69; H, 4.29; Cl, 10.38; N, 7.96%. Calcd for $C_{17}H_{15}ClN_2O_4$: C, 58.85; H, 4.32; Cl, 10.23; N, 8.07%. **5b** changed into **6b** in 45% yield on storage for 4 days. (b) The above reaction was carried out under reflux for 1 h to give the starting material (0.028 g), **3b** (1.005 g, 78%), and **6b** (0.228 g, 16%). (c) A solution of 1 (1.00 g) in abs ethanol (40 ml) was added into a mixture of the ester (1.00 g), sodium (0.40 g), and abs ethanol (60 ml) and stirred at room temperature for 1 days. Works-up gave **5b** (0.096 g, 11%), the starting material (0.347 g), **3b** (0.198 g, 24%), and **6b** (0.516 g, 56%).

*Reaction of **1** with Phenylacetonitrile.* (a) A solution of **1** (2.00 g) in dry dioxane (80 ml) was added into a mixture of phenylacetonitrile (2.00 g), sodium hydride (1.40 g), and dry dioxane (120 ml), stirred at room temperature for 1 day, and worked up as above to give **5c** (1.950 g, 65%) and **6c** (0.054 g, 2%), successively. **5c**: Needles (from methanol), mp 184—185 °C, NMR δ=1.40 (3H, t, J=7 Hz), 2.63 (1H, bq, J=9 Hz), 4.05 (1H, d, J=9 Hz), 4.35 (2H, q, J=7 Hz), 5.1—5.6 (2H, m), 6.42 (1H, d, J=9.5 Hz), 7.19 (1H, d, J=9.5 Hz), 7.32 (5H, s), 8.68 (1H, bs); UV_{max} 280 nm (log ε 3.89); IR: 3200 (NH), 2240 (C≡N), 1657 cm^{-1} (C=O). Found: C, 68.24; H, 4.92; Cl, 10.31; N, 7.79%. Calcd for $C_{20}H_{17}ClN_2O_2$: C, 68.07; H, 4.85; Cl, 10.05; N, 7.94%. **6c**: Yellow prisms (from benzene), mp 249.5—250 °C, NMR δ=1.50 (3H, t, J=7 Hz), 4.50 (2H, q, J=7 Hz), 7.4—7.9 (5H, m), 8.22 (2H, d, J=11 Hz), 8.73 (1H, d, J=11 Hz), 9.60 (1H, d, J=11 Hz);[6] UV_{max} 257 nm (log ε 4.46), 290 (4.25), 400 (4.45); IR 3190 (NH), 2200 (C≡N), 1707 cm^{-1} (C=O). Found: C, 68.14; H, 4.52; Cl, 10.21; N, 7.68%. Calcd for $C_{20}H_{15}ClN_2O_2$: C, 68.45; H, 4.31; Cl, 10.10; N, 7.98%. When a solution of **5c** in benzene was set aside for 4 days, **6c** was obtained in 24% yield. (b) The above reaction (**1** (1.00 g), dioxane (50 ml), the nitrile (0.50 g), and NaH (0.154 g) in dioxane (50 ml)) was carried out under reflux for 1 h to give the starting material (0.240 g), **2c** (0.882 g, 87%), and **6c** (0.025 g, 3%). **2c**: Yellow prisms (from benzene), mp 165—166 °C, NMR δ=1.43 (3H, t, J=7 Hz), 4.43 (2H, q, J=7 Hz), 6.57 (1H, s), 7.2—7.7 (5H, m), 7.8—8.2 (3H, m), 8.87 (1H, bd, J=9 Hz), 9.95 (1H, bd, J=9 Hz); UV_{max} 287 nm (log ε 4.59), 324 (3.90), 345 (3.58), 462 (2.97); IR 2250 (C≡N), 1675 cm^{-1} (C=O). Found: C, 75.63; H, 5.22; N, 8.58%. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86%. (c) A solution of **1** (1.00 g) in abs ethanol (30 ml) was added into a mixture of the nitrile (1.00 g), sodium (0.20 g), and abs ethanol (70 ml), heated under reflux for 1 h, and worked up to give **2c** (0.008 g, 1%), **5c** (1.05 g, 70%), and **6c** (0.025 g, 2%), successively.

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7) The NMR spectrum indicates that this compound is a mixture of geometrical isomers.