CONDENSATION OF ARYLIDENEISOPROPYLIDENEMALONATES WITH 3-CARBOXYPHENYLAMINOCYCLOHEXEN-2-ONES

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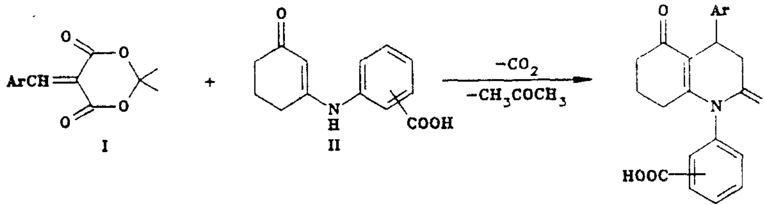
UDC 547.461.3'594.3'831.3'831.9.07

Reaction of arylideneisopropylidenemalonates with 3-carboxyphenylaminocyclohexen-2-ones leads to N-carboxyphenyl-4-aryloctahydroquinoline-2,5-diones with elimination of acetone and carbon dioxide.

In continuation of our study [1] of the reactivity of arylideneisopropylidenemalonates (I) we have investigated their condensation with 3-carboxyphenylaminocyclohexen-2-ones (II). The latter are the condensation products of dihydroresorcinol and aminobenzoic acid and are of interest from the viewpoint of biological activity. Condensation of I and II occurs in alcohol solvent to form N-carboxyphenyl-4-aryl-1,2,3,4,5,6,7,8-octahydroquinoline-2,5-diones. The reaction is accompanied by elimination of acetone and carbon dioxide.



I II III

Compound	COOH	Ar	Compound	COOH	Ar	Compound	COOH	Ar
IIIa	—	C_6H_5	IIIf	m-	p-$O_2NC_6H_4$	IIIk	o-	p-ClC_6H_4
IIIb	p-	C_6H_5	IIIg	o-	p-$O_2NC_6H_4$	IIIl	—	p-$CH_3OC_6H_4$
IIIc	o-	C_6H_5	IIIh	—	p-ClC_6H_4	IIIm	p-	p-$CH_3OC_6H_4$
IIId	—	p-$O_2NC_6H_4$	IIIi	p-	p-ClC_6H_4	IIIn	o-	p-$CH_3OC_6H_4$
IIIe	p-	p-$O_2NC_6H_4$	IIIj	m-	p-ClC_6H_4			

The compounds obtained (III) are light-colored materials, soluble in alkaline solutions and in highly polar solvents (Table 1).

Bearing in mind the interpretation of their IR spectra [2, 3] the maxima at 1690-1722 cm^{-1} in III can be assigned to stretching of the 5-carbonyl group. For compounds not containing the carboxyl group (IIIa, d, h, *l*) there are characteristic sharp and intense absorptions for stretching of the 2-carbonyl groups at 1641-1651 cm^{-1}. With the presence of a 2-carboxyl group in the N-phenyl ring a series of poorly defined maxima are observed in the range 1619-1711 cm^{-1} for the 2-carbonyl and carboxyl groups which can be related to the formation of molecular associates of III. The UV spectra of these compounds are practically identical and independent of the substituents in the 1 and 4 positions of the ring. Maxima were observed in the region 280-350 nm, analogous to the maxima of the starting 3-carboxyphenylaminocyclohexen-2-ones but shifted to shorter wavelength and with lower intensity.

PMR spectra of IIIa-n were complex, showing the protons of the carboxyl group, the phenyl substituents, and the 4-H [2, 3]. For interpretation of the 1.82-3.43 ppm portion of the spectrum, we have synthesized 7,7-dimethyl-1,4-diphenyl-1,2,3,4,5,6,7,8-octahydroquinoline-2,5-dione (IV) in which the methylene protons are isolated from one another. Comparison of the spectra for III and IV in the region 2.95-3.43 ppm identified these signals as those of the 3-CH_2. However, the remaining region of the spectrum (1.82-2.95 ppm) remained complex and could not be interpreted by the usual methods. The integrated peak intensity for these signals corresponded to six hydrogens.

Riga Technical University, Riga 226048. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 947-949, July, 1990. Original article submitted September 28, 1988; revision submitted August 9, 1989.

0009-3122/90/2607-0790$12.50

TABLE 1. N-Phenyl- and N-Carboxyphenyl-4-aryloctahydroquinoline-2,5-diones (IIIa-n)

Compound	Empirical formula	mp,* °C	IR spectrum, cm^{-1}		UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	PMR spectrum, ppm**						Yield, %
			5-CO	2-CO, COOH		COOH (b.s)	1,4-Ar^1, Ar^2, m	4-CH (1H)	OCH_3 (s, 3H)	3-CH_2 (m, 2H)	6,7,8-$(CH_2)_3$ (m, 6H)	
IIIa	$C_{21}H_{19}NO_2$	133...135	1689	1641	208 (22,0), 236 (6,60 sh), 298 (18,8)		7,17...7,43 (10H)	4,48 t		2,98...3,04	1,87...2,48	60
IIIb	$C_{22}H_{19}NO_4$	237...239	1716	1703, 1690 sh, 1655	200 (29,8), 223 (13,6 пл), 294 (18,3)	12,60	7,22...8,22 (9H)	4,53 t		3,04...3,12	1,97...2,46	61
IIIc	$C_{22}H_{19}NO_4$	172...174	1717	1654 sh,1619 sh	200 (36,4), 223 (10,7 sh), 298 (18,4)	10,29	7,04...8,24 (9H)	4,51 t		2,97...3,04	1,89...2,52	55
IIId	$C_{21}H_{18}N_2O_4$	190...192	1701	1651	205 (24,0), 217 (14,0 sh), 253 (13,6,sh), 288 (22,0)		7,00...8,20 (9H)	4,53...4,62 m		3,04...3,13	1,82...2,51	83
IIIe	$C_{22}H_{18}N_2O_6$	295...296	1722	1711sh,1690sh, 1655sh, 1638sh	205 (22,0), 218 (18,4 sh), 288 (23,2)	12,37	7,33...8,22 (8H)	4,41...4,50 m		3,17...3,43	1,91...2,87	78
IIIf	$C_{22}H_{18}N_2O_6$	296...297	1708	1689, 1676 sh, 1651 sh	204 (25,0), 221 (20,8), 290 (22,6)	12,40	7,52...8,20 (8H)	4,40...4,48 m		3,16...3,42	1,90...2,83	84
IIIg	$C_{22}H_{18}N_2O_6$	259...260	1705	1692sh,1680 sh, 1658, 1640	204 (25,6), 218 (20,0, sh), 293 (23,6)	12,20	7,00...8,18 (8H)	4,51...4,60 m		2,96...3,11	1,96...2,80	90
IIIh	$C_{21}H_{18}ClNO_2$	170...172	1704	1659	200 (30,3), 220 (16,5), 296 (17,8)		7,16...8,60 (9H)	4,33...4,41 m		2,90...2,97	1,86...2,43	63
IIIi	$C_{22}H_{18}ClNO_4$	248...250	1699sh	1679, 1658	201 (56,4), 222 (22,4), 297 (19,2)	11,92	7,09...8,20 (8H)	4,48 t		2,99...3,06	1,94...2,50	66
IIIj	$C_{22}H_{18}ClNO_4$	275...277	1719	1691sh,1676 sh 1651sh	206 (24,4), 212 (25,2), 297 (17,6)	12,22	7,18...8,03 (8H)	4,38...4,46 m		3,00...3,25	1,90...2,76	63
IIIk	$C_{22}H_{18}ClNO_4$	259...261	1720	1710sh,1695sh 1685sh,1656sh	203 (24,8), 222 (23,2), 297 (20,0)	11,98	7,00...8,10 (8H)	4,37...4,45 m		3,00...3,20	1,91...2,75	67
IIIℓ	$C_{22}H_{21}NO_3$	143...145	1693	1646	200 (28,7), 226 (12,8), 286 (12,5 sh), 296 (13,6)		6,74...7,42 (9H)	4,44 t	3,76	2,97...3,04	1,87...2,49	53
IIIm	$C_{23}H_{21}NO_5$	235...237	1720	1706sh, 1674, 1650	200 (28,7), 226 (12,8), 286 (12,5 sh), 296 (13,6)	11,05	6,73...8,13 (8H)	4,29...4,43 m	3,71	2,89...3,01	1,93...2,55	45
IIIn	$C_{23}H_{21}NO_5$	244...246	1717	1694sh,1679sh, 1658, 1642sh	205 (24,4), 222 (22,0), 284 (13,0 sh), 303 (17,8)	12,11	6,74...8,11 (8H)	4,33...4,41 m	3,73	2,90...3,16	1,92...2,75	45

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*Compounds IIIe, f, j were recrystallized from acetic acid, IIIb from ethanol–water, and the remaining compounds from ethanol.

**Solvents for IIIe, f, m DMSO-D_6, for the remaining compounds $CDCl_3$.

EXPERIMENTAL

IR spectra were recorded on a Specord IR-71 instrument, UV spectra on a Specord UV-vis in ethanol solvent, and PMR spectra on a Tesla BS 487-C (80 MHz) with TMS internal standard.

Elemental analytical data for C, H, N, and Cl for all of the newly synthesized compounds agreed with those calculated.

Arylideneisopropylidenemalonates were obtained by method [4], 3-(p-carboxyphenylamino)cyclohexen-2-one (p-II) by [5], and 3-phenylaminocyclohexen-2-one (II, no carboxyl group) by [6].

3-(m-Carboxyphenylamino)cyclohexen-2-one (m-II, $C_{13}H_{13}NO_3$). Dihydroresorcinol (5.6 g, 0.05 mole) and m-aminobenzoic acid (6.85 g, 0.05 mole) in 35 ml ethanol were refluxed for 10-15 min, and the precipitated solid filtered off and washed on the filter with ethanol to give 9.55 g (82.7%) of product. Crystallization from acetic acid gives finely crystalline yellow material with mp 244-245°C.

3-(o-Carboxyphenylamino)cyclohexen-2-one (o-II, $C_{13}H_{13}NO_3$). Dihydroresorcinol (5.6 g, 0.05 mole) and o-aminobenzoic acid (6.85 g, 0.05 mole) were refluxed in ethanol (30 ml) for 8 h. The oily product was treated with water (20 ml), placed in a refrigerator to yield a crystalline precipitate. Filtering and washing on the filter with ethanol gave 4.27 g (37.0%). Crystallization from acetic acid gave finely crystalline brown product with mp 174-176°C.

N-Phenyl- and N-Carboxyphenyl-4-aryl-1,2,3,4,5,6,7,8-octahydroquinoline-2,5-diones (IIIa-n). Malonate I (0.01 mole) and 3-phenylaminocyclohexen-2-one or compound II (0.01 mole) were refluxed in ethanol (15 ml) for 2 h on a water bath. The solution was evaporated, placed in a refrigerator, and the precipitated solid filtered off and recrystallized.

7,7-Dimethyl-1,4-diphenyl-1,2,3,4,5,6,7,8-octahydroquinoline-2,5-dione (IV, $C_{23}H_{23}NO_3$). Benzylideneisopropylidenemalonate (2.32 g, 0.01 mole) and 5,5-dimethyl-3-phenylaminocyclohexen-2-one [7] (2.15 g, 0.01 mole) were refluxed in ethanol (15 ml) on a water bath for 45 min. The solution was evaporated, placed in a refrigerator, and the precipitate of IV filtered, washed on the filter with ethanol and ether to give 1.92 g (55.6%). Crystallization from ethanol gives white crystals with mp 147-149°C. IR spectrum: 1705, 1654, 1621, 1596, 1559 sh, 1554, 1494 cm^{-1}. UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 206 (22.8), 237 (6.6, sh), 299 (17.8). PMR spectrum: 7.22-7.40 [10H, m, 1,4-$(C_6H_5)_2$]; 4.48 (1H, t, 4-CH); 2.99-3.05 (2H, m, 3-CH_2); 2.28 (2H, s, 6-CH_2); 2.03 (2H, s, 8-CH_2); 0.97 ppm [6H, d, J = 8 Hz, 7,7-$(CH_3)_2$].

LITERATURE CITED

1. M. F. Strozhev, I. É. Lielbriedis, and O. Ya. Neiland, *Khim. Geterotsikl. Soedin.*, No. 6, 786 (1990).
2. A. J. Gordon and R. A. Ford, *A Chemist's Companion* [Russian translation], Mir, Moscow (1976), p. 541.
3. *Determination of the Structure of Organic Compounds by Physical and Chemical Methods. Book 1* [Russian translation], Khimiya, Moscow (1967), p. 532.
4. P. Shuster, O. E. Polansky, and F. Wessely, *Monatsh. Chem.*, **95**, 53 (1964).
5. I. Jirkovsky, *Can. J. Chem.*, **52**, 55 (1974).
6. M. Regitz and H. Schwall, *Annalen*, **728**, 99 (1969).
7. P. Haas, *J. Chem. Soc.*, **89**, 187 (1906).