N-ALKYLATION OF 2,2,4-TRIMETHYL-1,2-DIHYDROQUINOLINE AND ITS DIMERIC ANALOGS UNDER INTERPHASE-CATALYSIS CONDITIONS

Kh. S. Shikhaliev and Zh. V. Shmyreva

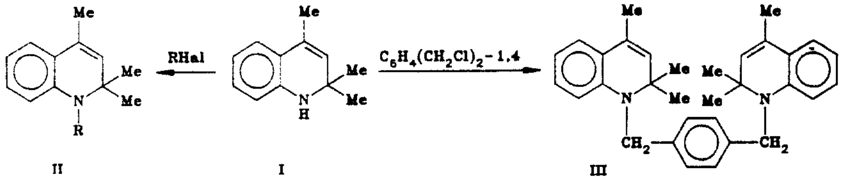
UDC 547.831.3:541.128.13

The possibility of the use of interphase catalysis for the synthesis of N-alkyl derivatives of 2,2,4-trimethyl-1,2-dihydroquinoline and its dimeric analogs was demonstrated. The effect of the nature of the alkylating agents on the reaction time and the yield of alkylation products was examined.

Heating of 2,2,4-trimethyl-1,2-dihydroquinoline (I), which is an effective antioxidant for rubbers and carotenoids [1], with methyl and ethyl iodides and subsequent treatment of the reaction mixture with alkali gave the N-methyl and N-ethyl derivatives of this heterocycle [2]. The use of other alkyl halides for the alkylation of quinoline I under similar conditions leads to difficult-to-separate mixtures of the starting compound and reaction products. In the present research we investigated the possibility of the alkylation of 2,2,4-trimethyl-1,2-dihydroquinoline and its dimeric analogs (IV) under interphase-catalysis conditions.

The alkylation of I with alkyl iodides, p-substituted benzyl chlorides, and allyl bromide was carried out in a two-phase system in the presence of catalytic amounts of tetrabutylammonium iodide. The substrate or a solution of the substrate in benzene was used as the organic phase, and 50% sodium hydroxide solution was used as the aqueous phase.

The reaction times and the yields of N-alkylation products under the same temperature conditions (40-60°C) have regularities that are characteristic for reactions of this type and are associated with the structure of the alkylating agent, the length of the hydrocarbon chain in the alkyl iodides, and the lability of the halogen atom (Table 1). Compound III, which contains two dihydroquinoline rings, was isolated when 1,4-bis(chloromethyl)benzene was used for the alkylation. Attempts to obtain similar compounds using methylene iodide, dibromoethane, and diiodoethane were unsuccessful.



II I III

II a $R=Me$, b $R=C_2H_5$, c $R=C_3H_7$, d $R=C_4H_9$, e $R=C_5H_{11}$, f $R=CH_2—CH=CH_2$, g $R=CH_2C_6H_5$, h $R=CH_2C_6H_4Cl$-*p*, i $R=CH_2C_6H_4NO_2$-*p*

Characteristic absorption bands of a quinoline ring at 1605 cm^{-1}, of a double bond in a dihydroquinoline fragment at 1630 cm^{-1}, and of stretching vibrations of a C—N bond at 1185 cm^{-1} are observed in the IR spectra of N-alkyl derivatives II and III (Table 1).

The singlet signal of the proton of an NH group at 3.6 ppm that is characteristic for starting I is absent in the PMR spectra of IIg-I and III (Table 2), but singlets of methylene protons at 4.42 ppm and signals of aromatic protons of a benzyl group appear in the spectra.

The alkylation of 2,2,4-trimethyl-1,2-dihydroquinoline dimer (IV) and its monobenzoyl derivatives (V) with methyl iodide was also carried out under interphase-catalysis conditions; exhaustive methylation product VI was isolated in the case of IV, while N-methyl

---

Lenin Komsomol State University, Voronezh 394693. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1091-1093, August, 1988. Original article submitted February 11, 1987; revision submitted November 10, 1987.

0009-3122/88/2408-0898$12.50

TABLE 1. Characteristics of the Synthesized Compounds

Compound	Reaction time, h	bp or mp, °C	n_D^{20}	IR spectrum,* cm^{-1}			Found, %			Empirical formula	Calculated, %			Yield, %
				C=C	C—N	C=O	C	H	N		C	H	N	
IIa	5	131...132 (4 hPa); 134...135 (6 hPa) [2]	1,5888	1632	1185	—	83,1	9,3	7,5	$C_{13}H_{17}N$	83,4	9,1	7,5	86
IIb	8	142...143 (8 hPa); 136...137 (6 hPa) [2]	1,5794	1632	1184	—	83,2	9,3	7,0	$C_{14}H_{19}N$	83,6	9,4	7,0	92
IIc	12	143...144 (5 hPa)	1,5702	1632	1185	—	83,2	9,5	6,6	$C_{15}H_{21}N$	83,7	9,8	6,5	82
IId	15	145...146 (3 hPa)	1,5631	1631	1185	—	83,4	10,3	6,2	$C_{16}H_{23}N$	83,8	10,0	6,1	70
IIe	18	154...155 (4 hPa)	1,5553	1630	1184	—	83,7	10,4	5,8	$C_{17}H_{25}N$	83,9	10,3	5,8	55
IIf	8	141...142 (4 hPa)	1,5839	1630, 1682	1182	—	84,9	8,6	6,7	$C_{15}H_{19}N$	84,5	8,9	6,6	92
IIg	10	72...73	—	1624	1178	—	86,9	7,7	5,1	$C_{19}H_{21}N$	86,7	8,0	5,3	62
IIh	10	80...81	—	1622	1185	—	76,1	6,9	4,6	$C_{19}H_{20}ClN$	76,6	6,7	4,7	40
IIi	4	85...86	—	1630	1184	—	74,4	6,7	9,4	$C_{19}H_{20}N_2O_2$	74,0	6,5	9,1	55
III	14	195...196	—	1632	1183	—	85,2	8,2	6,2	$C_{32}H_{36}N_2$	85,7	8,0	6,2	65
VI	16	150...151 148...149 [3]	—	1631	1198	—	82,6	9,3	7,6	$C_{26}H_{36}N_2$	83,0	9,6	7,4	48
VIIa	24	87...88	—	1632	1180	1694	82,4	8,5	5,7	$C_{35}H_{42}N_2O$	83,0	8,3	5,5	62
VIIb	24	59...60	—	1628	1182	1697	77,3	7,2	5,6	$C_{32}H_{35}ClN_2O$	77,0	7,0	5,6	60
VIIc	24	110...111	—	1632	1180	1698	75,1	6,7	8,6	$C_{32}H_{35}N_3O_3$	75,4	6,9	8,2	49

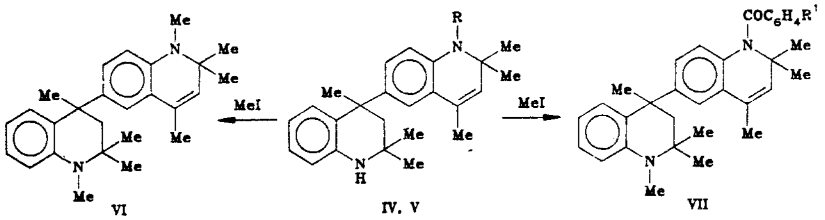
---

*IR spectrum of the NO_2 group: 1350, 1550 (for IIi); 1350, 1552 cm^{-1} (for VIIc).

TABLE 2. PMR Spectra of IIg-i and III

Compound	Chemical shifts, δ, ppm
IIg	1,36 (6H, s, $C(CH_3)_2$); 2,01 (3H, s, 4-CH_3); 4,46 (2H, s, CH_2); 5,25 (1H, s, C=CH); 6,11 ... 7,00 (4H, m, 5-, 6-, 7-, 8-H); 7,22 (5H, m, C_6H_5)
IIh	1,32 (6H, s, $C(CH_3)_2$); 2,01 (3H, s, 4-CH_3); 4,40 (2H, s, CH_2); 5,25 (1H, s, C=CH); 6,10 ... 7,00 (4H, m, 5-, 6-, 7-, 8-H); 7,19 (4H, s, C_6H_4)
IIi	1,29 (6H, s, $C(CH_3)_2$); 2,00 (3H, s, 4-CH_3); 4,50 (2H, s, CH_2); 5,26 (1H, s, C=CH); 5,93 ... 7,02 (4H, m, 5-, 6-, 7-, 8-H); 7,75 (4H, q, C_6H_4)
III	1,32 (12H, s, $C(CH_3)_2$); 1,98 (6H, h, 4-CH_3); 4,42 (4H, s, CH_2); 5,22 (2H, s, C=CH); 6,15 ... 6,98 (8H, m, 5-, 6-, 7-, 8-H); 7,17 (4H, s, C_6H_4)

derivatives VII are formed in the case of dimers V. The structures of VI and VII were confirmed by the results of elementary analysis and IR spectral data (Table 1).



IV R=H; V R=$COC_6H_4R^1$; V, VII a R^1=C_3H_7, b R^1=Cl, c R^1=NO_2

EXPERIMENTAL

The IR spectra of films of the liquid compounds and mineral-oil suspensions of the solid compounds were obtained with a UR-20 spectrometer. The PMR spectra of solutions in CCl_4 were recorded with a Varian-100/15 spectrometer (100 MHz) with tetramethylsilane as the internal standard.

Starting dimers IV and Va-c were obtained by the methods in [3, 4].

The course of the reactions and the individuality of the substances obtained were monitored by TLC (Silufol UV-254, elution with benzene, development with iodine vapors).

The characteristics of the synthesized compounds are presented in Tables 1 and 2.

Alkylation of 2,2,4-Trimethyl-1,2-dihydroquinoline (I). A mixture of 37.5 g (210 mmole) of I, 250 mmole of the corresponding alkyl or benzyl halide, 85 ml of 50% NaOH solution, and 0.74 g (2 mmole) of tetrabutylammonium iodide was stirred at 40-60°C until the reaction was complete, after which the reaction mixture was poured into 200 ml of water, and the aqueous mixture was extracted with ether (three 50-ml portions). The ether extracts were washed with water and dried. The residue after removal of the ether by distillation was distilled in vacuo in the case of IIa-f, which were light-yellow mobile liquids, whereas it was recrystallized from hexane in the case of IIg-i and III.

Methylation of Dimer IV and Its Benzoyl Derivatives V. A mixture of 15 mmole of IV or V, 2.5 ml (35 mmole) of methyl iodide, 20 ml of 50% NaOH solution, 70 ml of benzene, and 0.37 g (1 mmole) of tetrabutylammonium iodide was stirred for 16-24 h at 40-50°C, after which the benzene layer was separated, washed with water, and dried. The solvent was removed by distillation, and the residue was recrystallized from ethanol.

LITERATURE CITED

1. O. T. Kasaikina, A. B. Gagarina, Yu. A. Ivanov, É. G. Rozantsev, and N. M. Émanuél', Izv. Akad. Nauk SSSR, Ser. Khim., No. 10, 2247 (1975).
2. J. Reddelein and A. Thurm, Chem. Ber., 65, 1151 (1933).
3. J. Elliot and H. Dunathan, Tetrahedron., 19, 833 (1963).
4. É. M. Gurova, M. M. Zablotskaya, I. K. Marshakov, and Zh. V. Shmyreva, USSR Author's Certificate No. 1082785; Byull. Izobret., No. 12, 83 (1984).