SYNTHESIS OF STABLE FUNCTIONALLY SUBSTITUTED NITRILE OXIDES OF THE AROMATIC SERIES

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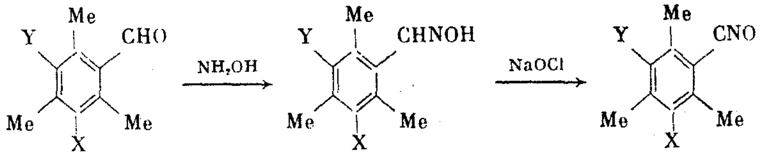
Stable functionally substituted mononitrile oxides were obtained from the previously obtained sterically hindered aldehydes of the mesitylene series. The previously unknown bisnitrile oxide was also synthesized from triethylbenzene; the compound is an effective crosslinking agent. The synthesis was carried out via the stage of oximation and oxidation of the oxime by sodium hypochlorite.

During the investigation of the formylation of aromatic substrates under the conditions of the Riher reaction (dichloromethyl alkyl ethers in the presence of Lewis acids), we obtained [1] a series of sterically hindered aromatic aldehydes, derivatives of mesitylene containing an additional functional group, and also dialdehydes from p-xylene, mesitylene, durene, and the previously unknown 2,4,6-triethylisophthalic dialdehyde from 1,3,5-triethylbenzene. It was of interest, using the above compounds, to obtain a series of nitrile oxides, having functional groups such as ester, ether, hydroxyl, acetyl, and nitrile oxide groups in the aromatic ring. The stability of nitrile oxides is ensured by the presence of two screening alkyl substituents in the o,o'-position to the nitrile oxide group. Compounds of this type are of preparative value: various functionally substituted cycloadducts can be obtained from them, while bisnitrile oxides can be used as effective crosslinking agents. Only some representatives of nitrile oxides of this type have been described until now [2-4].

The synthesis of nitrile oxides included the step of oximation of the aldehydes and oxidation of the oximes to the desired end product, carried out by standard methods [5, 6].

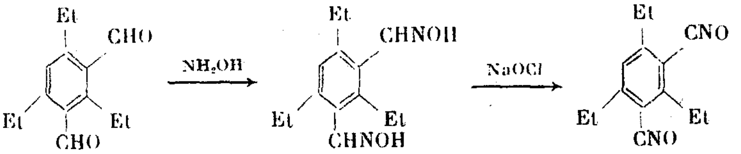


(I)—(VII)   (VIII)—(XIV)

Y = H; X = CH_2OMe (I), (VIII); OH (II), (IX); Ac (III), (X), CO_2Me(V), (XII), CO_2Et (VI), (XIII); CO_2Pr-*i* (VII), (XIV); X = Y = CH_2OMe (IV), (XI).

The new scheme proposed by us in [1] of the synthesis of 2,4,6-trimethylisophthalic dialdehyde and 2,3,5,6-tetramethylterepthalic dialdehyde from mesitylene and durol makes novel stable dinitrile oxides available, the synthesis of which from dialdehydes has been previously described in [7, 8].

Thus, from 1,3,5-triethylbenzene we obtained 2,4,6-triethylisophthalodinitrile oxide for the first time.



(XV)   (XVI)

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TABLE 1. Characteristics of Aldoximes (I)-(VII), (XV), and Nitrile Oxides (VIII)-(XIV), (XVI)

Compound	Yield, %	Mp, °C (hexane)[a]	Found/Calculated, %			Empirical formula
			C	H	N	
(I)	75	133–136, 92–96[b]	69,42/69,53	8,32/8,29	6,90/6,76	$C_{12}H_{17}NO_2$
(II)	75	168–171	67,00/67,01	7,39/7,30	7,87/7,81	$C_{10}H_{13}NO_2$
(III)[c]	81	Oil				
(IV)	74	129–130,5	66,73/66,90	8,62/8,42	5,50/5,57	$C_{14}H_{21}NO_3$
(V)	95	88–90	64,66/65,14	6,91/6,83	6,12/6,33	$C_{12}H_{15}NO_3$
(VI)	98	77–78	66,72/66,35	7,20/7,28	5,71/5,95	$C_{13}H_{17}NO_3$
(VII)	89	113–115	67,16/67,35	7,70/7,67	5,61/5,61	$C_{14}H_{19}NO_3$
(VIII)	82	50–50,5	70,38/70,21	7,38/7,38	6,88/6,82	$C_{12}H_{15}NO_2$
(IX)[d]	30	78–82	74.63/74,42	6,83/6,83	8.50/8,69	$C_{10}H_{11}NO_2$
(X)[e]	55	115–118	70,74/70,91	6,55/6,44	6,95/6,89	$C_{12}H_{13}NO_2$
(XI)	80	128–129.5	66,47/66,90	7,94/8,42	7.08/6,57	$C_{14}H_{19}NO_3$
(XII)	92	102–103,5	65.57/65,74	6,16/5,96	6,22/6,39	$C_{12}H_{13}NO_3$
(XIII)	83	103–103,5	66,75/66,93	6,50/6,48	5,51/5,00	$C_{13}H_{15}NO_3$
(XIV)	78	91,5–92	67,71/67,99	7,00/6.93	5,57/5,66	$C_{14}H_{17}NO_3$
(XV)	74	122–123.5			10,96/11,28	$C_{14}H_{20}N_2O_2$
(XVI)	75	93–96	69,05/68.83	6.61/6,60	11,22/11,47	$C_{14}H_{16}N_2O_2$

a) Compounds (IV), (XI), (XV) were recrystallized from a mixture of hexane with benzene, (II) – from 50% aqueous ethanol, (XVI) – from a mixture of alcohol and $CHCl_3$.

b) The aldoxime is formed in two isomeric forms (syn and anti).

c) The compound could not be isolated in an analytically pure state.

d) The compound was obtained by the oxidation of the aldoxime by N-bromosuccinimide according to the method in [9].

e) The product was isolated by column chromatography on silica gel (eluent $CHCl_3$).

All the nitrile oxides obtained are stable compounds and readily enter the 1,3-dipolar cycloaddition reaction with compounds containing multiple bonds.

EXPERIMENTAL

The PMR spectra were run on Bruker WM 250 (250 MHz) and Bruker AC 200P (200 MHz) radiospectrometers in deuterochloroform. The mass spectra were obtained on a Varian MAT CH-6 mass spectrometer with direct introduction of the sample to the ionic source, ionizing voltage 70 eV, emission current 0.1 mA. The IR spectra were recorded on a Perkin–Elmer 577 spectrophotometer (KBr tablets).

Preparation of Aldoximes (I)-(VII), (XV). Solutions of 0.2 mole of NaOH in 10 ml of H_2O and 0.2 mole of $NH_2OH\cdot HCl$ in 25 ml of H_2O [for compound (XV) a double amount of the reagents was used] were added successively at 50°C to a solution of 0.1 mole of the aldehyde

TABLE 2. PMR Spectra of Aldoximes (I)-(VII), (XV), and Nitrile Oxides (VIII)-(XIV), (XVI)

Compound	δ, ppm								
	2-Me	4-Me	6-Me	H_{Ar}	—CH	—OH	$-CH_2O$	—OMe	additional signals
(I) (syn)	2,37	2,23	2,31	6,93	–	7,65 br.s	4,48	3,41	
(I) (anti)	2,39	2,33	2,37	6,92	8,49	7,50 br.s	4,48	3,41	
(II)	2,31	2,24	2,31	6,85	8,39	–	–	–	OH does not appear
(III)	2,34	2,20	2,36	6,92	8.35	–	–	–	2,48 $(COCH_3)$
(IV)	2,35	2,45	2,35	–	8,33	8,48 br.s	4,50	3,42	
(V)	2,35	2,28	2,31	6.94	8,35	8,42 br.s	–	3,91	
(VI)	2,41	2,30	2,39	6,95	8,15	8,46 br.s	4.41 q	–	1,40 t (Me)
(VII)	2.35	2,29	2,32	6,94	8,20	8,36 br.s	–	–	5,31 m (CH) 1,38 d (Me)
(VIII)	2,52	2,39	2,42	6,97	–	–	4,44	3,42	
(IX)	2,37	2,25	2,37	6,89	–	–	–	–	4,61 (OH)
(X)	2,45	2,25	2,36	6,97	–	–	–	–	2,48 $(COCH_3)$
(XI)	2,53	2,46	2,53	–	–	–	4.46	3,42	
(XII)	2,45	2,29	2,41	6,98	–	–	–	3,94	
(XIII)	2,45	2,33	2,40	6,97	–	–	4,41 q	–	1,40 t (Me)
(XIV)	2,45	2,30	2,42	6,97	–	–	–	–	5,31 m (CH) 1,38 d (Me)
(XV)	1,12t	1,19t	1,19t	7,02	7.86	8,40	–	-	2,76 q $(2\text{-}CH_2)$; 2,69 q (4-and $6\text{-}CH_2$)
(XVI)	1.33 t	1,31 t	1,31 t	7,08	–	–	–	–	2,93 q $(2\text{-}CH_2)$; 2,81 (4- and $6\text{-}CH_2$)

in 300-400 ml of EtOH. The reaction mixture was boiled for 4 h, the solvent was distilled, the residue was treated with 50-100 ml of $CHCl_3$ and 100 ml of water, the organic layer was separated and washed with water (3 × 200 ml). After the distillation of $CHCl_3$, the residue was recrystallized from the corresponding solvent (Tables 1 and 2).

Preparation of Nitrile Oxides (VIII)-(XIV), (XVI). A solution of 0.1 mole aldoxime in 150-250 ml of CH_2Cl_2 was added at 5-7°C in the course of 5-10 min to a vigorously stirred aqueous solution of 0.25 mole of 10-15% sodium hypochloride containing 8-10% NaOH, cooled to 5-7°C (for aldoxime (XV) 0.5 mole of sodium hypochlorite was used). The mixture was stirred vigorously for 1 h with gradual increase of the temperature to 15°C, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 ml). The combined organic layer was washed with water (4 × 100 ml) and after distillation of the solvent in vacuo, the residue was recrystallized (see Tables 1 and 2).

LITERATURE CITED

1. A. P. Yakubov, D. V. Tsyganov, L. I. Belen'kii, and M. M. Krayushkin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 7 (1991).
2. Ch. Grundmann and P. Grünanger, The Nitrile Oxides, Springer-Verlag, Berlin (1971).
3. K. R. Rao, T. Srinivasan, and P. B. Sattur, Heterocycles, 27, No. 3, 683 (1989).
4. J. N. Kim and E. K. Pyu, Heterocycles, 31, No. 4, 663 (1990).
5. C. Grundmann and J. M. Dean, J. Org. Chem., 30, 2803 (1965).
6. G. A. Lee, Synthesis, 508 (1982).
7. C. Grundmann and R. Richter, J. Org. Chem., 33, 2308 (1968).
8. C. Grundmann and J. M. Dean, Angew. Chem., 76, No. 15, 682 (1964).
9. L. S. Dyankova, Tr. Khim.-Farm. Inst. (Bulgaria), 15, 55-61 (1985).