Potassium Fluoride-Promoted Reaction of (2-Chloro-2-nitroethenyl)benzenes with 1,3-Dicarbonyl Compounds. A General Synthesis of 6,6-Dimethyl-2-nitro-3-phenyl-3,5,6,7-tetrahydro-4(2*H*)benzofuranones and some Analogs

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A convenient procedure to prepare in good yields 6,6-dimethyl-2-nitro-3-phenyl-3,5,6,7-tetrahydro-4(2*H*)-benzofuranones starting from (2-chloro-2-nitroethenyl)benzenes and 5,5-dimethyl-1,3-cyclohexanedione in the presence of potassium fluoride is reported. This method also proved efficient with other 1,3-dicarbonyl compounds, and has been successfully extended to 1,3-cyclohexanedione, 2,5-pentanedione, dibenzoylmethane and ethyl acetoacetate.

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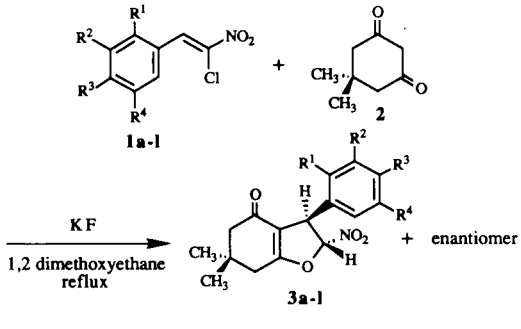
In the course of our studies on the synthetic applications of (2-chloro-2-nitroethenyl)benzenes [1-3], we have now investigated the reaction of these compounds with 1,3-dicarbonyl derivatives. We have chosen to carry out these attempts in the presence of potassium fluoride since this weak base has been successfully used, on several occasions, by Yoshikoshi and co-workers to catalyse Michael additions of β-dicarbonyl compounds and simple nitroolefins to provide acylfurans [4,5], tricarbonyl derivatives [4,6], 2-phenylthio-2,3-dihydrofurans [7-9] or (hydroxyimino)dihydrofurans [8], depending on the reaction conditions and on the nature of the reagents involved.

We report herein that the potassium fluoride-promoted condensation of (2-chloro-2-nitroethenyl)benzenes **1a-l** with 5,5-dimethyl-1,3-cyclohexanedione (**2**) in refluxing 1,2-dimethoxyethane affords, in good yields, 6,6-dimethyl-2-nitro-3-phenyl-3,5,6,7-tetrahydro-4(2*H*)-benzofuranones **3a-l** exclusively in the *trans* configurations (Scheme 1).

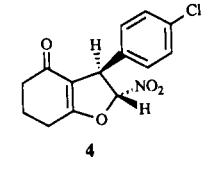
Scheme 1



1a-l **2** **3a-l**

1,3	R^1	R^2	R^3	R^4
a	H	H	H	H
b	Cl	H	H	H
c	H	Cl	H	H
d	H	H	Cl	H
e	NO_2	H	H	H
f	H	NO_2	H	H
g	H	H	NO_2	H
h	OCH_3	H	H	H
i	H	OCH_3	H	H
j	H	H	OCH_3	H
k	H	OCH_3	OCH_3	OCH_3
l	H	H	$-(CH=CH)_2-$	

The scope of this reaction has been explored with a number of substrates including compounds bearing electron-donating or electron-withdrawing groups in various positions and was found to be quite general (Table 1). Furthermore, with the 4-chloro derivative **1d** selected as a typical compound of this class, we also established that other 1,3-dicarbonyl reagents such as 1,3-cyclohexanedione, 2,5-pentanedione, dibenzoylmethane and ethyl acetoacetate undergo similar reactions to give respectively the corresponding 2,3-dihydro-2-nitro-3-phenylfurans **4-7** (Table 1).



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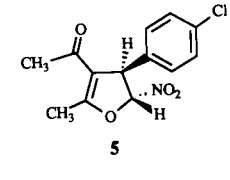

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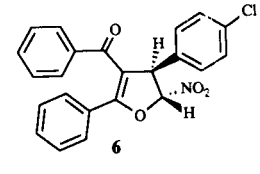

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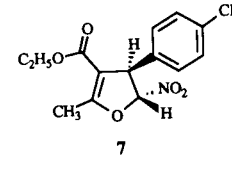

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The ^1H nmr spectra of the condensation products **3a-l** and **4-7** reported in Table 2 are indicative of a *trans* configuration according to the small values measured for the coupling constants between the vicinal protons H_2 and H_3 (J = 1.5-2.9 Hz). A single crystal X-ray analysis of 4-acetyl-3-(4-chlorophenyl)-2,3-dihydro-5-methylfuran (**5**), chosen as a representative of this class of compounds, confirms the *trans* stereochemistry as depicted in Figure 1. With regard to the nmr of compounds **3a-l** and **4**, it is also worth pointing out that unusually large ^5J coupling constants (about 2 Hz in certain cases such as **3b**, **3c**, **3e** or **3f**) exist between the proton located in the 3-position and those located in the 7-position. This fact, added to the non-equivalence of the two H_7 protons, is responsible for the

Table 1

Preparation on Compounds 3a-l and 4-7

Compound	Yield %	Melting point (°C) (recrystallization solvent)	Empirical Formula (Molecular weight)	Analysis % Calcd./(Found) C	H	N
3a	76	109-110 (cyclohexane)	$C_{16}H_{17}NO_4$ (287.3)	66.89 (66.69)	5.96 (5.84)	4.87 (4.89)
3b	71	141-142 (cyclohexane)	$C_{16}H_{16}ClNO_4$ (321.8)	59.73 (59.60)	5.01 (4.92)	4.35 (4.20)
3c	87	123-124 (heptane)	$C_{16}H_{16}ClNO_4$ (321.8)	59.73 (59.79)	5.01 (5.00)	4.35 (4.30)
3d	82	141-142 (cyclohexane)	$C_{16}H_{16}ClNO_4$ (321.8)	59.73 (59.61)	5.01 (4.95)	4.35 (4.34)
3e	72	159-160 [a] (benzene-heptane)	$C_{16}H_{16}N_2O_6$ (332.3)	57.83 (57.75)	4.85 (4.85)	8.43 (8.25)
3f	90	176-177 (benzene-heptane)	$C_{16}H_{16}N_2O_6$ (332.3)	57.83 (57.62)	4.85 (4.82)	8.43 (8.40)
3g	87	150-152 (benzene-cyclohexane)	$C_{16}H_{16}N_2O_6$ (332.3)	57.83 (57.90)	4.85 (4.83)	8.43 (8.21)
3h	70	99-100 (hexane)	$C_{17}H_{19}NO_5$ (317.3)	64.34 (64.17)	6.03 (6.07)	4.41 (4.35)
3i	82	92-93 (hexane)	$C_{17}H_{19}NO_5$ (317.3)	64.34 (64.55)	6.03 (6.09)	4.41 (4.36)
3j	77	100-101 (hexane)	$C_{17}H_{19}NO_5$ (317.3)	64.34 (64.21)	6.03 (6.08)	4.41 (4.37)
3k	75	122-123 (cyclohexane)	$C_{19}H_{23}NO_7$ (377.4)	60.47 (60.49)	6.14 (6.00)	3.71 (3.62)
3l	78	191-192 (benzene-cyclohexane)	$C_{20}H_{19}NO_4$ (337.4)	71.20 (71.01)	5.68 (5.67)	4.15 (4.07)
4	78	109-110 (cyclohexane)	$C_{14}H_{12}ClNO_4$ (293.7)	57.25 (57.13)	4.12 (4.16)	4.77 (4.71)
5	69	122-123 (hexane-benzene)	$C_{13}H_{12}ClNO_4$ (281.7)	55.43 (55.56)	4.29 (4.19)	4.97 (4.94)
6	55	100-103 (hexane-benzene)	$C_{23}H_{16}ClNO_4$ (405.8)	68.07 (68.30)	3.97 (3.92)	3.45 (3.44)
7	52	79-80 (hexane)	$C_{14}H_{14}ClNO_5$ (311.7)	53.94 (54.09)	4.53 (4.57)	4.49 (4.40)

[a] Allotropic change at 145-149°.

complexity observed for the signal of H_3. A ^5J coupling constant is similarly observable between the protons of the CH_3 group and H_3 in the spectra of compounds **5** and **7**.

It should be noted that some 2,3-dihydro-2-nitrofurans were previously reported in the literature [10-14]. However, shortly afterwards, it was published by the same authors [15,16] that the products described in their earlier papers were actually nitrocyclopropane derivatives and not 2,3-dihydro-2-nitrofurans as they initially indicated.

EXPERIMENTAL

Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. The proton nuclear magnetic resonance spectra were recorded at 90 MHz using a Varian EM 390 spectrometer, with tetramethylsilane as the internal standard. Elemental analyses were carried out by the "Service d'Analyse du CNRS, Vernaison". Silica gel (Merck, 230-400 mesh) was used

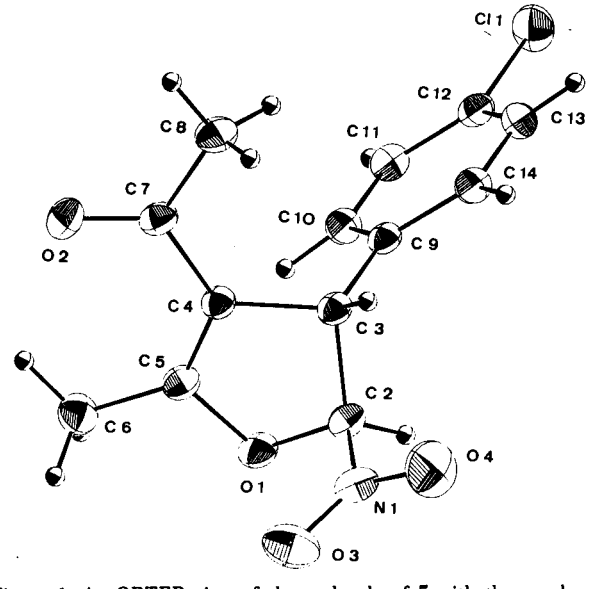

Figure 1. An ORTEP view of the molecule of **5** with the numbering scheme adopted for the X-ray analysis. The thermal ellipsoids are drawn at a 30% probability level.

Table 2

^{1}H-NMR Spectral Data of **3a-l** and **4-7** δ (ppm), Deuteriochloroform

Compound	
3a	1.20 (br s, 6H), 2.30 (br s, 2H), 2.53-2.70 (m, 2H), 4.51-4.66 (m, 1H), 5.93 (d, 1H, J = 2.1 Hz), 7.03-7.47 (m, 5H)
3b	1.20 (s, 3H), 1.22 (s, 3H), 2.32 (s, 2H), 2.62 (br d, 2H, J = 1.9 Hz), 4.98-5.12 (m, 1H), 5.94 (d, 1H, J = 2.2 Hz), 6.83-7.55 (m, 4H)
3c	1.20 (br s, 6H), 2.33 (s, 2H), 2.65 (br d, 2H, J = 1.8 Hz), 4.53-4.67 (m, 1H), 5.92 (d, 1H, J = 2.1 Hz), 7.02-7.43 (m, 4H)
3d	1.18 (s, 6H), 2.28 (br s, 2H), 2.55-2.70 (m, 2H), 4.51-4.63 (m, 1H), 5.88 (d, 1H, J = 2.1 Hz), 7.12 and 7.32 (AA'BB' system, 4H)
3e	1.18 (s, 3H), 1.20 (s, 3H), 2.30 (s, 2H), 2.59 (d, 2H, J = 2.1 Hz), 5.20-5.35 (m, 1H), 6.09 (d, 1H, J = 2.9 Hz), 7.08-7.28 (m, 1H), 7.33-7.71 (m, 2H), 7.92-8.11 (m, 1H)
3f	1.22 (br s, 6H), 2.32 (s, 2H), 2.67 (br d, 2H, J = 1.8 Hz), 4.65-4.80 (m, 1H), 5.94 (d, 1H, J = 2.1 Hz), 7.42-7.76 (m, 2H), 7.93-8.31 (m, 2H)
3g	1.20 (br s, 6H), 2.30 (br s, 2H), 2.55-2.73 (m, 2H), 4.61-4.76 (m, 1H), 5.94 (d, 1H, J = 2.0 Hz), 7.37 and 8.20 (AA'BB' system, 4H)
3h	1.22 (br s, 6H), 2.32 (s, 2H), 2.52-2.65 (m, 2H), 3.85 (s, 3H), 4.80-4.93 (m, 1H), 5.94 (d, 1H, J = 2.5 Hz), 6.70-7.00 (m, 3H), 7.10-7.43 (m, 1H)
3i	1.20 (br s, 6H), 2.30 (s, 2H), 2.55-2.70 (m, 2H), 3.79 (s, 3H), 4.51-4.65 (m, 1H), 5.92 (d, 1H, J = 2.0 Hz), 6.65-6.95 (m, 3H), 7.13-7.40 (m, 1H)
3j	1.20 (br s, 6H), 2.29 (s, 2H), 2.55-2.68 (m, 2H), 3.77 (s, 3H), 4.48-4.62 (m, 1H), 5.88 (d, 1H, J = 2.1 Hz), 6.85 and 7.08 (AA'BB' system, 4H)
3k	1.22 (br s, 6H), 2.32 (br s, 2H), 2.58-2.71 (m, 2H), 3.80 (s, 3H), 3.82 (s, 6H), 4.46-4.58 (m, 1H), 5.90 (d, 1H, J = 2.0 Hz), 6.38 (s, 2H)
3l	1.19 (s, 3H), 1.21 (s, 3H), 2.30 (br s, 3H), 2.57-2.71 (m, 2H), 4.66-4.82 (m, 1H), 5.98 (d, 1H, J = 2.1 Hz), 7.13-7.93 (m, 7H)
4	2.00-2.53 (m, 4H), 2.65-2.88 (m, 2H), 4.51-4.66 (m, 1H), 5.85 (d, 1H, J = 2.0 Hz), 7.12 and 7.30 (AA'BB' system, 4H)
5	2.06 (s, 3H), 2.52 (d, 3H, J = 1.5 Hz), 4.57-4.70 (m, 1H), 5.65 (d, 1H, J = 1.8 Hz), 7.15 and 7.35 (AA'BB' system, 4H)
6	4.88 (d, 1H, J = 1.5 Hz), 5.90 (d, 1H, J = 1.5Hz), 6.97-7.58 (m, 14H)
7	1.12 (t, 3H, J = 7.3 Hz), 2.50 (d, 3H, J = 1.5 Hz), 4.05 (q, 2H, J = 7.3 Hz), 4.49-4.65 (m, 1H). 5.70 (d, 1H, J = 1.9 Hz), 7.14 and 7.32 (AA'BB' system, 4H)

Table 3

Crystal and Refinement Parameters for Compound **5**

Empirical formula	$C_{13}H_{12}ClNO_4$
Fomula weight	281.7
Crystal dimensions (mm)	0.45 x 0.40 x 0.30
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	7.409 (2)
b(Å)	11.998 (4)
c(Å)	14.694 (6)
β(°)	101.26 (3)
V (Å^3)	1281 (1)
Z	4
Dcalc (g.cm^{-3})	1.46
μ (cm^{-1})	3.0
F (000)	584
Scan type	w-2 Θ
Scan width	0.80 + 0.34 tan Θ
radiation, λ(Å)	MoKα, 0.71073
Θ range (°)	1.5 - 25
Number of independent measured reflections	3082
Number of total used reflections I ≥ 3 σ I	2188
Number of refined parameters	211
Weighting scheme W	1
$R = S\|\Delta F\|/\Sigma\|F_o\|$	0.0393
$R_w = [\Sigma w(\Delta F)^2/\Sigma wF_o^2]^{1/2}$	0.0367

for column chromatography. Commercially available reagents and solvents were used without further purification. Starting materials **1a-l** were prepared according to a method described in a previous communication [3].

General Procedure for the Preparation of 6,6-Dimethyl-2-nitro-3-phenyl-3,5,6,7-tetrahydro-4(2*H*)-benzofuranones **3a-l**.

A mixture of 5,5-dimethyl-1,3-cyclohexanedione (**2**, 1.4 g, 10 mmoles), (2-chloro-2-nitroethenyl)benzene **1a-l** (5 mmoles), anhydrous 1,2-dimethoxyethane (25 ml) and potassium fluoride

Table 4

Atomic and Thermal Parameters for Compound **5**

Atom	x/a	y/b	z/c	U (equiv)
C1(1)	0.9254(1)	0.06688(6)	0.13575(5)	0.0607
O(1)	0.8937(2)	0.1717(1)	0.6176(1)	0.0436
O(2)	0.3137(2)	0.1418(2)	0.5269(1)	0.0537
O(3)	0.8910(3)	0.3572(2)	0.7043(1)	0.0759
O(4)	0.9326(4)	0.4568(2)	0.5904(2)	0.0855
N(1)	0.9128(3)	0.3687(2)	0.6262(1)	0.0516
C(2)	0.9159(3)	0.2651(2)	0.5651(2)	0.0413
C(3)	0.7514(3)	0.2692(2)	0.4836(1)	0.0358
C(4)	0.6157(3)	0.2013(2)	0.5257(1)	0.0355
C(5)	0.7077(3)	0.1447(2)	0.5985(1)	0.0402
C(6)	0.6580(4)	0.0590(2)	0.6607(2)	0.0530
C(7)	0.4165(3)	0.1961(2)	0.4891(1)	0.0400
C(8)	0.3431(4)	0.2641(3)	0.4053(2)	0.0530
C(9)	0.7965(3)	0.2178(2)	0.3965(1)	0.0338
C(10)	0.8225(3)	0.1035(2)	0.3897(2)	0.0408
C(11)	0.8635(3)	0.0575(2)	0.3104(2)	0.0424
C(12)	0.8774(3)	0.1253(2)	0.2368(1)	0.0402
C(13)	0.8529(3)	0.2390(2)	0.2414(2)	0.0437
C(14)	0.8142(3)	0.2843(2)	0.3218(2)	0.0404

Table 5

Bond Lenghts (Å) and Angles (°) for Compound **5**

Cl(1)	C(12)	1.741(2)	
O(1)	C(2)	1.389(3)	
O(1)	C(5)	1.389(2)	
O(2)	C(7)	1.216(3)	
O(3)	N(1)	1.198(3)	
O(4)	N(1)	1.202(3)	
N(1)	C(2)	1.536(3)	
C(2)	C(3)	1.533(3)	
C(3)	C(4)	1.516(3)	
C(3)	C(9)	1.515(3)	
C(4)	C(5)	1.336(3)	
C(4)	C(7)	1.470(3)	
C(5)	C(6)	1.470(3)	
C(7)	C(8)	1.489(3)	
C(9)	C(10)	1.391(3)	
C(9)	C(14)	1.384(3)	
C(10)	C(11)	1.376(3)	
C(11)	C(12)	1.373(3)	
C(12)	C(13)	1.379(3)	
C(13)	C(14)	1.380(3)	
C(5)	O(1)	C(2)	107.2(2)
O(4)	N(1)	O(3)	124.8(2)
C(2)	N(1)	O(3)	119.2(2)
C(2)	N(1)	O(4)	116.0(2)
N(1)	C(2)	O(1)	108.1(2)
C(3)	C(2)	O(1)	107.3(2)
C(3)	C(2)	N(1)	109.3(2)
C(4)	C(3)	C(2)	98.8(2)
C(9)	C(3)	C(2)	112.0(2)
C(9)	C(3)	C(4)	113.6(2)
C(5)	C(4)	C(3)	108.9(2)
C(7)	C(4)	C(3)	124.9(2)
C(7)	C(4)	C(5)	126.2(2)
C(4)	C(5)	O(1)	112.0(2)
C(6)	C(5)	O(1)	113.4(2)
C(6)	C(5)	C(4)	134.6(2)
C(4)	C(7)	O(2)	122.0(2)
C(8)	C(7)	O(2)	120.7(2)
C(8)	C(7)	C(4)	117.2(2)
C(10)	C(9)	C(3)	121.1(2)
C(14)	C(9)	C(3)	120.4(2)
C(14)	C(9)	C(10)	118.4(2)
C(11)	C(10)	C(9)	120.8(2)
C(12)	C(11)	C(10)	119.5(2)
C(11)	C(12)	Cl(1)	119.5(2)
C(13)	C(12)	Cl(1)	119.4(2)
C(13)	C(12)	C(11)	121.1(2)
C(14)	C(13)	C(12)	118.9(2)
C(13)	C(14)	C(9)	121.3(2)

(0.58 g, 10 mmoles) was gently refluxed for 24 hours under inert atmosphere. The mixture was allowed to cool to room temperature. An insoluble material was then filtered out by suction and thoroughly rinsed with dichloromethane. The combined filtrates were evaporated under reduced pressure to leave a residue which was chromatographed on silica gel [100 g, eluting with dichloromethane except for **3k** where a mixture dichloromethane/ethyl acetate (75:25) was used]. Evaporation of the solvent followed by recrystallization provided analytically pure compounds **3a-l** in the reported yields (Table 1).

The 3-(4-chlorophenyl)-2-nitro-3,5,6,7-tetrahydro-4(2*H*)-benzofuranone (**4**), 4-acetyl-3-(4-chlorophenyl)-2,3-dihydro-5-methyl-2-nitrofuran (**5**), 4-benzoyl-3-(4-chlorophenyl)-2,3-dihydro-2-nitro-5-phenylfuran (**6**), and the ethyl ester of the 2-(4-chlorophenyl)-2,3-dihydro-5-methyl-2-nitro-4-furancarboxylic acids (**7**) were synthesized following the same procedure starting from the appropriate 1,3-dicarbonyl compounds. The chromatographies were performed by eluting with pure dichloromethane for compounds **4** and **5**, with a dichloromethane/hexane (50:50) mixture for compound **6**, or with a dichloromethane/hexane (75:25) mixture for compound **7**.

Single Crystal X-ray Analysis of **5**.

Crystallographic and refinement parameters are summarized in Table 3.

The data were collected on a Nonius CAD 4 diffractometer using graphite-monochromated MoK_α radiation. Two standard reflexions were measured every two hours, no change was observed. Absorption correction was made by an empirical method based on the psi-scan of two reflections (minimum-maximum correction factor: 1.00-1.07). The structure was solved with CRYSTALS [17] program using direct methods and refined by least squares techniques. The hydrogen atom positions were derived from difference maps. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were refined isotropically. Atoms were corrected from anomalous dispersion and a secondary extinction correction was applied. The largest peaks on the final difference map were of heights +0.29 and -0.31 e $Å^{-3}$. The final atomic parameters for non-hydrogen atoms are given in Table 4. Bond lengths and bond angles are listed in Table 5.

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REFERENCES AND NOTES

[1] D. Dauzonne and R. Royer, *Synthesis*, 1020 (1987).

[2] D. Dauzonne and R. Royer, *Synthesis*, 339 (1988).

[3] D. Dauzonne and P. Demerseman, *Synthesis*, 66 (1990).

[4] T. Yanami, M. Kato and A. Yoshikoshi, *J. Chem. Soc., Chem. Commun.*, 726 (1975).

[5] T. Yanami, A. Ballatore, M. Miyashita, M. Kato and A. Yoshikoshi, *J. Chem. Soc., Perkin Trans. I*, 1144 (1978).

[6] T. Yanami, M. Kato and A. Yoshikoshi, *Synthesis*, 407 (1980).

[7] M. Miyashita, T. Kumazawa and A. Yoshikoshi, *J. Chem. Soc., Chem. Commun.*, 362 (1978).

[8] M. Miyashita, T. Kumazawa and A. Yoshikoshi, *J. Org. Chem.*, **45**, 2945 (1980).

[9] M. Miyashita, T. Kumazawa and A. Yoshikoshi, *J. Org. Chem.*, **49**, 3728 (1984).

[10] Ya. S. Bolovich, V. V. Perekalin and A. S. Sopova, *Dokl. Akad. Nauk. SSSR*, **134**, 1083 (1960).

[11] A. S. Sopova, V. V. Perekalin and Ya. S. Bolovich, *Zh. Obshch. Khim.*, **31**, 1528 (1961).

[12] A. S. Sopova, V. V. Perekalin and O. I. Yurchenko, *Zh. Obshch. Khim.*, **33**, 2140 (1963).

[13] A. S. Sopova, V. V. Perekalin and V. M. Lebednova, *Zh. Obshch. Khim.*, **33**, 2143 (1963).

[14] A. S. Sopova, V. V. Perekalin and O. I. Yurchenko, *Zh. Obshch. Khim.*, **34**, 1188 (1964).

[15] A. S. Sopova, O. I. Yurchenko and V. V. Perekalin, *Zh. Org. Khim. SSSR*, **1**, 1707 (1965).

[16] H. H. Baer and L. Urbas in The Chemistry of the Nitro and Nitroso Groups, Part 2, S. Patai, ed, Interscience Publishers, New York, 1970, p 143.

[17] J. R. Carruthers and D. W. Watkin, CRYSTALS, An Advanced Crystallographic Computer Program, Chemical Crystallographic Laboratory, Oxford University, 1985.