Monatsh Chem (2013) 144:375–379
DOI 10.1007/s00706-012-0825-2

ORIGINAL PAPER

An improved, safe, and efficient conversion of triarylpyrylium perchlorates to corresponding cyanodienones using Amberlite IRA 910[CN]

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Received: 10 December 2011 / Accepted: 10 July 2012 / Published online: 7 August 2012

Abstract Triarylpyrylium perchlorates are readily converted into new aromatic cyanodienones by using cyanide impregnated on anion exchange resin as a safe and efficient reagent.

Keywords Anion exchange resin · Cyanodienones · Green chemistry · Heterocycles · Nucleophilic additions

Introduction

Butenolides are ubiquitous moieties in many natural products [1–5]. These compounds are potent antibiotics [6, 7], often show interesting antimicrobial activity [8], appear as substructures in peptide analogues and HIV-1 protease inhibitors [9, 10], and can also be main materials for the development of new asymmetric methodologies [11, 12].

The reaction of substituted pyrylium salts **1** with aqueous alkali cyanides affords the corresponding cyanodienones **2**, which are utilized as key intermediates for butenolides **3** [13] (Scheme 1).

Therefore, the design of new and improved methods for the synthesis of cyanodienones is of interest. The majority of the work reported in this area has concentrated on alkylpyrylium compounds [13, 14], and in the case of arylpyrylium, this reaction is restricted only to triphenylpyrylium perchlorates [15]; in this sense, the reaction of various triarylpyrylium perchlorates with aqueous sodium cyanide is still a challenge to investigate. In continuation of our ongoing work to develop selective, preparatively and synthetically useful methodology for the preparation [16], application [17, 18], and transformation of pyrylium and thiopyrylium salts [19–23], besides the importance of biological active aromatic butenolides [24–28], we decided to synthesize new aromatic cyanodienones from the reaction of cyanide anion with various triarylpyrylium perchlorates carrying electron-donating and -withdrawing groups in the *para* position of substituted phenyl rings.

Because of the toxicity of the cyanide anion, which leads to vomiting, convulsions, loss of consciousness, and eventual death [29–31], and in the interest of developing green chemistry, we also tried to use a new strategy where the cyanide anion is impregnated on anion exchange resin as a safe and efficient reagent. Resins are very important in circumventing major environmental problems and serious separation difficulties encountered with many current methods. In addition, they can be used as effective catalysts in various organic reactions, e.g., azidation of α,β-unsaturated ketones [32], protection of carbonyl groups [33], reduction of 4-nitrophenol [34], sampling and preservation of sulfoxyanions in natural waters [35], and highly regioselective conversion of epoxides to β-hydroxynitriles [36].

Results and discussion

Reactions of triarylpyrylium perchlorates **4** containing electron-donating and -withdrawing groups in the *para* position of substituted phenyl rings with sodium cyanide afford the corresponding cyanodienones **6** via intermediate 2-cyanopyrans **5** which could not be isolated (Scheme 2).

Electronic supplementary material The online version of this article (doi:10.1007/s00706-012-0825-2) contains supplementary material, which is available to authorized users.

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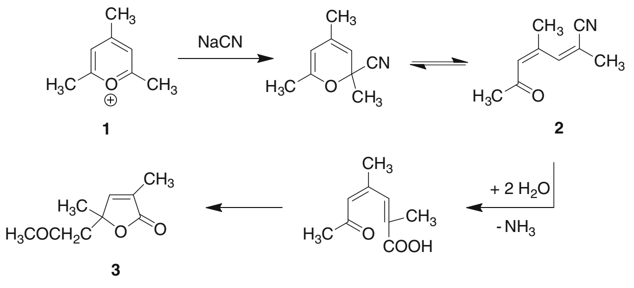
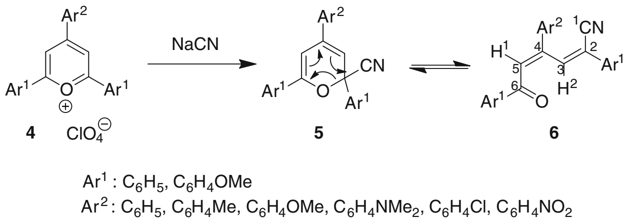


Scheme 1



Ar^1 : C_6H_5, C_6H_4OMe
Ar^2 : C_6H_5, C_6H_4Me, C_6H_4OMe, $C_6H_4NMe_2$, C_6H_4Cl, $C_6H_4NO_2$

Scheme 2

Preliminary tests were carried out to survey the requisite reaction conditions and establish the modifications required for this methodology. Triphenylpyrylium perchlorate was chosen as the model compound to identify and optimize the reaction conditions.

Initially, reaction of the model compound with sodium cyanide was followed in different solvent. In the presence of protic solvents such as ethanol, the reaction was not successful and noticeable amounts of starting material remained intact. In low polarity solvents such as tetrahydrofuran or dichloromethane, starting material could not completely dissolve. In acetonitrile the reaction was very fast and gave the corresponding cyanodienone in 78 % yield within 30 min, so acetonitrile appeared to be the solvent of choice giving the best results.

Following these tests, the relative molar ratio of nucleophile and substrate was also optimized. The best results were obtained when 2 mmol of nucleophile and 1 mmol of substrate were used.

The scope and generality of this process are illustrated with various triarylpyrylium perchlorates and new aromatic cyanodienones were synthesized in good yields (Table 1). The structures of all products were determined from their spectral data (IR, ^{1}H NMR, ^{13}C NMR).

The data in Table 1 clearly show that electron-donating groups cause the reactions to become slow (e.g., entries 1–6). This may be rationalized by considering the fact that these groups decrease the positive charge on the α-position of the heterocyclic ring. Stronger electron-donating groups exhibit longer reaction times. In contrast electron-withdrawing groups (e.g., entries 7 and 8) accelerate the reaction.

As stated earlier, because of the toxicity of the cyanide anion in the traditional method and in order to shed more light on the mechanism, these conversions were done in the presence of Amberlite IRA 910[CN] as an improved reagent. This reagent was prepared by simple mixing sodium cyanide and Amberlite IRA 910[Cl] in H_2O. The capacity of the resin was determined with a potentiometric method. Then the conversion of various triarylpyrylium perchlorates to the corresponding cyanodienones was investigated in the presence of this reagent and in the traditional method (Table 1).

This resin has a highly developed structure with sites that easily trap the starting materials and accelerate the reaction. In particular the workup and handling of the reaction were very easy and the pure products could be isolated with simple filtering; the filtered resin could be used several times without any loss in its capacity and efficiency.

In conclusion, we describe a novel and general protocol for the synthesis of new aromatic cyanodienones from the reaction of triarylpyrylium perchlorates with Amberlite IRA 910[CN] as a safe and highly efficient reagent. This environmentally friendly methodology offers several advantages including decrease of toxicity, easy workup and handling, short reaction times, and reusability of the resin.

Table 1 Conversion of various triarylpyrylium salts into corresponding cyanodienones in acetonitrile at room temperature (Scheme 2)

Entry	Ar^1	Ar^2	Product	Reaction time with NaCN	Reaction time with IRA 910[CN]	Yield/%
1	C_6H_5	C_6H_5	**6a**	30 min	25 min	78
2	C_6H_5	*p*-Me-C_6H_4	**6b**	1 h	40 min	81
3	C_6H_5	*p*-MeO-C_6H_4	**6c**	4 h	30 min	91
4	*p*-MeO-C_6H_4	*p*-Me-C_6H_4	**6d**	10 h	40 min	95
5	*p*-MeO-C_6H_4	*p*-MeO-C_6H_4	**6e**	16 h	50 min	93
6	C_6H_5	*p*-Me_2N-C_6H_4	**6f**	23 h	2 h	88
7	C_6H_5	*p*-Cl-C_6H_4	**6g**	25 min	20 min	70
8	C_6H_5	*p*-NO_2-C_6H_4	**6h**	20 min	15 min	72

Experimental

Chemicals were purchased from Fluka, Merck, and Aldrich chemical companies. Monitoring of the reactions was accomplished by TLC. IR spectra were obtained on a Bomen MB:102 FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz Bruker spectrometer using $CDCl_3$ as the solvent and TMS as the internal standard. All triarylpyrylium perchlorates were synthesized from the corresponding aldehydes and ketones by the method previously described [37, 38] (and references therein).

*General procedure for the reaction of triarylpyrylium perchlorates **4** with sodium cyanide*

The triarylpyrylium perchlorates (1 mmol) were stirred with sodium cyanide (2 mmol) at room temperature in acetonitrile (10 mmol). The reactions were monitored by TLC using ether/*n*-hexane (1:4) as eluent. After completion of the reaction, the solvent was evaporated under vacuum and the residue was worked up in aqueous ethyl acetate (in order to remove excess cyanide), then recrystallized from EtOH.

Preparation of polymer-supported cyanide anion

Amberlite IRA 910[Cl] (100 g) was stirred for 12 h with 32 g sodium cyanide in 450 cm^{3} water. The resin was filtered off, washed successively with water, and dried under vacuum at 40 °C (Fig. 1).

Estimation the capacity of the polymer-supported cyanide

A sample of 1.00 g dry resin was stirred for 12 h with 830 mg potassium iodide in 10 cm^{3} water. The resin was filtered off, washed with water, and the combined filtrate and washings titrated against silver nitrate solution using a potentiometer. The capacity generally was found to be 1.4 mmol/g (Fig. 2).

*General procedure for the reaction of triarylpyrylium perchlorates **4** with cyanide impregnated on anion exchange resin*

The triarylpyrylium salts (1 mmol) were stirred with cyanide impregnated on Amberlite IRA 910 (2 mmol) at room temperature in acetonitrile (10 mmol) and the reactions were followed by TLC (similar to the previous procedure). After completion of the reaction, the resin was removed by filtering and the product recrystallized from EtOH.

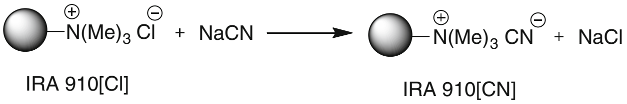


Fig. 1 Preparation of polymer-supported cyanide anion from IRA 910[Cl]

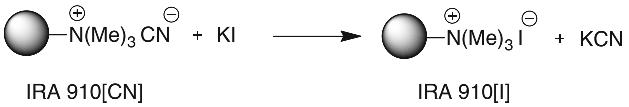


Fig. 2 Estimation the capacity of the polymer-supported cyanide via anion exchange of IRA 910[CN] with iodide

(2Z,4E)-6-Oxo-2,4,6-triphenyl-2,4-hexadienenitrile (**6a**, $C_{24}H_{17}NO$)
Yield 78 %; yellow crystals; m.p.: 103–105 °C (from EtOH); IR (neat): $\bar{\nu}$ = 2,218 (CN), 1,645 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (s, 1H, H^{1}), 7.45–8.05 (m, 15H, Ar–H), 8.40 (s, 1H, H^{2}) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.9 (C-2), 119.6 (C-1), 126.2 (C-5), 126.9, 128.8, 129.1, 129.2, 129.4, 129.5, 130.3, 130.6, 133.6 (ArC), 134.1, 138.8, 139.4 (ArC$_q$), 141.8 (C-3), 151.9 (C-4), 190.6 (C-6) ppm.

(2Z,4E)-4-(4-Methylphenyl)-6-oxo-2,6-diphenyl-2,4-hexadienenitrile (**6b**, $C_{25}H_{19}NO$)
Yield 81 %; yellow crystals; m.p.: 116–118 °C (from EtOH); IR (neat): $\bar{\nu}$ = 2,218 (CN), 1,644 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.46 (s, 3H, CH_3), 7.32 (s, 1H, H^{1}), 7.45–8.04 (m, 14H, Ar–H), 8.37 (s, 1H, H^{2}) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (CH_3), 115.7 (C-2), 118.9 (C-1), 124.8 (C-5), 126.4, 128.4, 128.6, 128.7, 129.0, 129.7, 129.8, 133.1 (ArC), 133.7, 136.1, 138.5, 140.7 (ArC$_q$), 142.0 (C-3), 151.6 (C-4), 190.2 (C-6) ppm.

(2Z,4E)-4-(4-Methoxyphenyl)-6-oxo-2,6-diphenyl-2,4-hexadienenitrile (**6c**, $C_{25}H_{19}NO_2$)
Yield 91 %; yellow crystals; m.p.: 112–114 °C (from EtOH); IR (neat): $\bar{\nu}$ = 2,218 (CN), 1,643 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 3H, OCH_3), 7.30 (s, 1H, H^{1}), 7.00–7.02, 7.43–8.03 (m, 14H, Ar–H), 8.35 (s, 1H, H^{2}) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 114.4 (C-5), 115.2 (C-2), 118.8 (C-1), 123.5, 126.4, 128.3, 128.7, 129.0, 129.8, 130.2 (ArC), 131.2 (ArC$_q$), 133.0 (ArC), 133.6, 138.6 (ArC$_q$), 142.5 (C-3), 151.3 (ArC$_q$), 161.5 (C-4), 190.1 (C-6) ppm.

(2Z,4E)-2,6-Bis(4-methoxyphenyl)-4-(4-methylphenyl)-6-oxo-2,4-hexadienenitrile (**6d**, $C_{27}H_{23}NO_3$)
Yield 95 %; yellow crystals; m.p.: 129–131 °C (from EtOH); IR (neat): $\bar{\nu}$ = 2,217 (CN), 1,638 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (s, 3H, CH_3), 3.86, 3.89 (2 s, 6H, OCH_3), 7.25 (s, 1H, H^{1}), 6.95–6.99, 7.23–7.28, 7.43–8.02 (m, 12H, Ar–H), 8.31 (s, 1H, H^{2}) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (CH_3), 55.4,

55.5 (OCH_3), 113.9 (C-5), 114.4 (ArC), 115.8 (C-2), 118.3 (C-1), 124.9 (ArC), 126.4 (ArC_q), 127.9, 128.6, 129.6, 130.7 (ArC), 131.7, 136.6 (ArC_q), 139.5 (C-3), 140.3 (ArC_q), 151.1 (C-4), 160.9, 163.5 (ArC_q), 188.7 (C-6) ppm.

(2Z,4E)-2,4,6-Tris(4-methoxyphenyl)-6-oxo-2,4-hexadienenitrile (**6e**, $C_{27}H_{23}NO_4$)

Yield 93 %; yellow crystals; m.p.: 131–133 °C (from EtOH); IR (neat): $\bar{\nu} = 2{,}218$ (CN), 1,636 (CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.87$, 3.88, 3.90 (3 s, 9H, OCH_3), 7.22 (d, $J = 1.0$ Hz, 1H, H^1), 6.95–7.01, 7.49–8.03 (m, 12H, Ar–H), 8.29 (d, $J = 1.0$ Hz, 1H, H^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 55.2$, 55.3, 55.4 (OCH_3), 113.7 (C-5), 113.9, 114.4 (ArC), 115.9 (C-2), 118.2 (C-1), 123.7 (ArC), 126.4 (ArC_q), 127.8, 127.9, 129.2, 130.3 (ArC), 141.0 (ArC_q), 150.8 (C-3), 157.1, 160.9, 161.2 (ArC_q), 163.4 (C-4), 188.7 (C-6) ppm.

(2Z,4E)-4-[4-(Dimethylamino)phenyl]-6-oxo-2,6-diphenyl-2,4-hexadienenitrile (**6f**, $C_{25}H_{19}N_2O$)

Yield 88 %; red crystals; m.p.: 174–176 °C (from EtOH); IR (neat): $\bar{\nu} = 2{,}215$ (CN), 1,628 (CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.07$ (s, 6H, $N(CH_3)_2$), 7.30 (d, $J = 1.0$ Hz, 1H, H^1), 6.74–6.76, 7.41–8.03 (m, 14H, Ar–H), 8.32 (d, $J = 1.0$ Hz, 1H, H^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 40.1$ ($N(CH_3)_2$), 111.9 (C-5), 116.1 (C-2), 118.0 (C-1), 119.8 (ArC), 125.7 (ArC_q), 126.4, 128.2, 128.6, 129.0, 129.5, 130.0, 132.5 (ArC), 133.8, 139.2 (ArC_q), 144.0 (C-3), 151.9 (ArC_q), 152.2 (C-4), 190.0 (C-6) ppm.

(2Z,4E)-4-(4-Chlorophenyl)-6-oxo-2,6-diphenyl-2,4-hexadienenitrile (**6g**, $C_{24}H_{16}ClNO$)

Yield 70 %; yellow crystals; m.p.: 109–111 °C (from EtOH); IR (neat): $\bar{\nu} = 2{,}218$ (CN), 1,647 (CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.29$ (s, 1H, H^1), 7.41–8.03 (m, 14H, Ar–H), 8.35 (s, 1H, H^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 115.5$ (C-2), 119.4 (C-1), 126.0 (C-5), 126.4, 128.4, 128.8, 129.1, 129.3, 129.9 (ArC), 130.0 (ArC_q), 133.3, 133.4 (ArC), 136.4, 137.3, 138.3 (ArC_q), 140.9 (C-3), 150.2 (C-4), 190.0 (C-6) ppm.

(2Z,4E)-4-(4-Nitrophenyl)-6-oxo-2,6-diphenyl-2,4-hexadienenitrile (**6h**, $C_{24}H_{16}N_2O_3$)

Yield 72 %; brown crystals; m.p.: 151–153 °C (from EtOH); IR (neat): $\bar{\nu} = 2{,}218$ (CN), 1,651 (CO), 1,518, 1,345 (NO_2) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.30$ (s, 1H, H^1), 7.24, 7.44–8.34 (m, 14H, Ar–H), 8.39 (s, 1H, H^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 115.4$ (C-2), 120.0 (C-1), 124.2 (C-5), 126.5, 128.3, 128.5, 128.9, 129.2, 129.7, 130.4 (ArC), 133.1 (ArC_q), 133.7 (ArC), 137.9 (ArC_q), 139.4 (C-3), 145.2, 148.5 (ArC_q), 148.8 (C-4), 189.8 (C-6) ppm.

Acknowledgments This work was supported by the Research Council at the University of Shahid Chamran. Thanks are expressed to Mr. A.T. Balaban for providing some references.

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