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Electrogenerated base-promoted synthesis of tetrahydrobenzo[*b*]pyran derivatives

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Abstract—An efficient and convenient synthesis of tetrahydrobenzo[*b*]pyrans is described, using an electrogenerated base of the anion of malononitrile in a one-pot, three component condensation of an aromatic aldehyde, an active methylene compound and dimedone. The reaction is carried out at room temperature in acetonitrile with the use of a sacrificial magnesium anode in a single-compartment cell.

The 4*H*-pyran group is a constituent of the structures of a series of natural products[1,2] with interesting biological and pharmacological activities[3] such as anti-coagulant, anticancer, spasmolytic, anti-anaphylactic, etc.[4] Furthermore, these compounds can be employed as pigments,[5] photoactive materials[6] and utilized as potential biodegradable agrochemicals.[7] The importance of these compounds has led many workers to synthesize them using methods including microwave[8] and ultrasonic irradiation[9] or by using tetrabutylammonium bromide,[10] (*S*)-proline,[11] rare earth perfluorooctanoates[12] and hexadecyltrimethylammonium bromide[13] as basic catalysts in one-pot reactions. Each of the above methods has its own merits, while some are plagued by limitations of poor yields, difficult work-up and toxic effluents.

For about 20 years there has been a growing realization that the deliberate cathodic generation of anionic bases, in aprotic solvents, might be preparatively convenient and offer possibilities for control of such factors as base strength and base concentration. The term probase has come into regular use to describe a compound which on reduction is converted into an intermediate that acts predominantly as a base, and which is described as an electrogenerated base (EGB).

Recently, it was found that chemical bases could be replaced with an electrogenerated base to promote reactions in higher yields.[14] Electroorganic reactions proceed generally smoothly with easy work-up and do not require the use of harsh conditions such as high temperatures and expensive reagents. To date, no reports have been published on the electrosynthesis of 4*H*-pyrans and as a part of our program devoted to the electrosynthesis of heterocycles[15] we decided to investigate the electrochemical synthesis of 4*H*-pyrans. Herein we report the synthesis of various 4*H*-pyran derivatives via electroreduction of malononitrile at a platinum electrode (Scheme 1).

Electrosynthesis at constant current of malononitrile (**1**), aryl aldehydes **2** and dimedone (**3**) proceeded in an undivided cell containing a Pt electrode as cathode and a sacrificial magnesium strip as anode to avoid electrochemical side reactions.

The reactions were complete after 4–5 h and afforded high yields of the desired products under mild conditions. All the products are known and were identified by comparison of their physical (mp) and spectroscopic data (IR and ^{1}H NMR) with those reported (Table 1).

We presume that the electrogenerated base in the present case is the anion of malononitrile, formed along with dihydrogen by the reduction of malonitrile **1** at the platinum cathode.[19] The reaction proceeds via initial formation of cyanoolefin **6** through condensation of aryl aldehyde **2** and the electrogenerated anion of malononitrile **5**. Cyanoolefin **6** then reacts with the active

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Keywords: Electrosynthesis; Pyran; Malononitrile; Electrogenerated.

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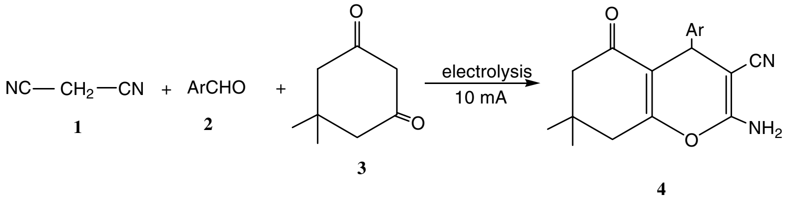
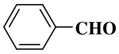
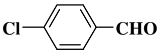
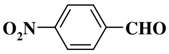
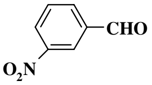
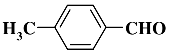
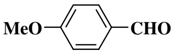
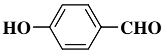
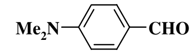


Scheme 1.

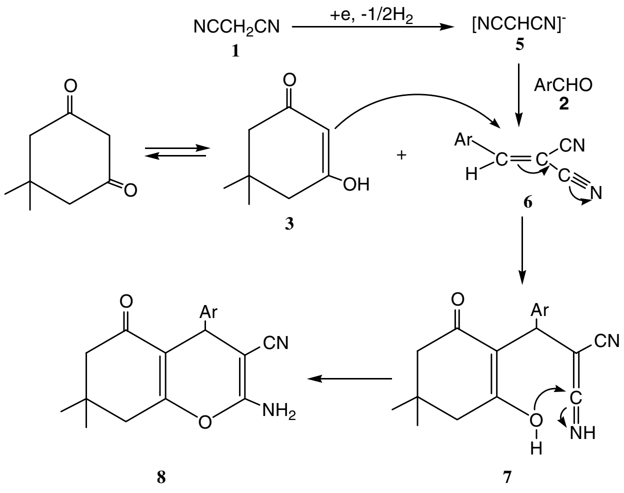
Table 1. Electrosynthesis of 2-amino-4*H*-pyran derivatives in acetonitrile

Entry	Aldehyde	Product	Yield[a] (%)	Charge (F)	Mp (°C)	
					Found	Reported
1		**8a**	96	1.51	224	226–228[16]
2		**8b**	95	1.57	206	207–209[16]
3		**8c**	94	1.79	179	177–178[13]
4		**8d**	96	1.67	210	208–211[13]
5		**8e**	94	1.60	213	214–216[13]
6		**8f**	95	1.70	201	198–200[16]
7		**8g**	89	1.83	205	206–208[17]
8		**8h**	91[18]	1.71	198–200	—

[a] Yields refer to isolated products.

methylene moiety of **3** giving intermediate **7**. Next, intermediate **7** is cyclized to give the expected products **8** (Scheme 2).

Under these conditions, it was found that the three-component condensations were very effective for the preparation of 4*H*-pyran derivatives (Table 1). The electronic nature of the substituents on the aromatic ring showed no particular effect on the conversion. The total charge involved during the electrochemical process was calculated from the duration of electrolysis at a constant current of 10 mA. As the reaction proceeded, the current used was small and the total charge passed was correspondingly small.



Scheme 2.

In conclusion, the use of an EGB in comparison with conventional chemistry[16,20] has advantages such as (i) in situ generation of base, (ii) a one-pot reaction in excellent yields under milder conditions, (iii) avoidance of polluting or hazardous chemicals or the addition of base or probase, and involves an easy work-up procedure.

Electroorganic synthesis of 2-amino-4H-pyrans: In a typical procedure, an acetonitrile (50 ml) solution of malononitrile (1.1 mmol), dimedone (1.1 mmol), aromatic aldehyde (1 mmol) and tetraethylammonium perchlorate (0.1 M) as supporting electrolyte in an undivided cell fitted with a consumable magnesium anode and a Pt sheet as cathode was subjected to electrolysis at room temperature and at a constant current (10 mA). The progress of the reaction was monitored by thin layer chromatography. The reaction time was in all the cases about 4–5 h. The resulting precipitate was filtered and recrystallized from an ethanol–water (3:1) mixture. All the products were characterized by spectroscopy and from physical data.

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